Sowerbutts, A. M., Lal, S., Sremanakova, J., Clamp, A., Todd, C., Jayson, G. C., Teubner, A., Raftery, A. M., Sutton, E. J., Hardy, L., & Burden, S. (2018). Home parenteral nutrition for people with inoperable malignant bowel obstruction. *Cochrane Database of Systematic Reviews*, *2018*(8), [CD012812]. https://doi.org/10.1002/14651858.CD012812.pub2

Cochrane Library

Cochrane Database of Systematic Reviews

Home parenteral nutrition for people with inoperable malignant bowel obstruction (Review)

Sowerbutts AM, Lal S, Sremanakova J, Clamp A, Todd C, Jayson GC, Teubner A, Raftery AM, Sutton EJ, Hardy L, Burden S

Sowerbutts AM, Lal S, Sremanakova J, Clamp A, Todd C, Jayson GC, Teubner A, Raftery AM, Sutton EJ, Hardy L, Burden S.
Home parenteral nutrition for people with inoperable malignant bowel obstruction.
Cochrane Database of Systematic Reviews 2018, Issue 8. Art. No.: CD012812.
DOI: 10.1002/14651858.CD012812.pub2.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Home parenteral nutrition for people with inoperable malignant bowel obstruction

Anne Marie Sowerbutts[1], Simon Lal[2], Jana Sremanakova[1], Andrew Clamp[3], Chris Todd[1], Gordon C Jayson[3], Antje Teubner[2], Anne-Marie Raftery[4], Eileen J Sutton[5], Lisa Hardy[6], Sorrel Burden[1]

[1]School of Health Sciences, The University of Manchester, and Manchester Academic Health Science Centre, Manchester, UK. [2]Intestinal Failure Unit, Salford Royal Foundation Trust, Salford, UK. [3]Division of Cancer Services, The Christie NHS Foundation Trust and University of Manchester, Manchester, UK. [4]Supportive/Palliative Care Team, The Christie NHS Foundation Trust, Manchester, UK. [5]Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK. [6]Department of Nutrition & Dietetics, Manchester University NHS Foundation Trust, Manchester, UK

Contact address: Anne Marie Sowerbutts, School of Health Sciences, The University of Manchester, and Manchester Academic Health Science Centre, Oxford Road, Manchester, M13 9PL, UK. annemarie.sowerbutts@manchester.ac.uk.

Editorial group: Cochrane Gynaecological, Neuro-oncology and Orphan Cancer Group.
Publication status and date: New, published in Issue 8, 2018.

Citation: Sowerbutts AM, Lal S, Sremanakova J, Clamp A, Todd C, Jayson GC, Teubner A, Raftery AM, Sutton EJ, Hardy L, Burden S. Home parenteral nutrition for people with inoperable malignant bowel obstruction. *Cochrane Database of Systematic Reviews* 2018, Issue 8. Art. No.: CD012812. DOI: 10.1002/14651858.CD012812.pub2.

ABSTRACT

Background

People with advanced ovarian or gastrointestinal cancer may develop malignant bowel obstruction (MBO). They are able to tolerate limited, if any, oral or enteral (via a tube directly into the gut) nutrition. Parenteral nutrition (PN) is the provision of macronutrients, micronutrients, electrolytes and fluid infused as an intravenous solution and provides a method for these people to receive nutrients. There are clinical and ethical arguments for and against the administration of PN to people receiving palliative care.

Objectives

To assess the effectiveness of home parenteral nutrition (HPN) in improving survival and quality of life in people with inoperable MBO.

Search methods

We searched the following electronic databases: Cochrane Central Register of Controlled Trials (CENTRAL; 2018, Issue 1), MEDLINE (Ovid), Embase (Ovid), BNI, CINAHL, Web of Science and NHS Economic Evaluation and Health Technology Assessment up to January 2018, ClinicalTrials.gov (http://clinicaltrials.gov/) and in the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal (http://apps.who.int/trialsearch/). In addition, we handsearched included studies and used the 'Similar articles' feature on PubMed for included articles.

Selection criteria

We included any studies with more than five participants investigating HPN in people over 16 years of age with inoperable MBO.

Data collection and analysis

We extracted the data and assessed risk of bias for each study. We entered data into Review Manager 5 and used GRADEpro to assess the quality of the evidence.

Main results

We included 13 studies with a total of 721 participants in the review. The studies were observational, 12 studies had only one relevant treatment arm and no control and for the one study with a control arm, very few details were given. The risk of bias was high and the certainty of evidence was graded as very low for all outcomes. Due to heterogeneity of data, meta-analysis was not performed and therefore the data were synthesised via a narrative summary.

The evidence for benefit derived from PN was very low for survival and quality of life. All the studies measured overall survival and 636 (88%) of participants were deceased at the end of the study. However there were varying definitions of overall survival that yielded median survival intervals between 15 to 155 days (range three to 1278 days). Three studies used validated measures of quality of life. The results from assessment of quality of life were equivocal; one study reported improvements up until three months and two studies reported approximately similar numbers of participants with improvements and deterioration. Different quality of life scales were used in each of the studies and quality of life was measured at different time points. Due to the very low certainty of the evidence, we are very uncertain about the adverse events related to PN use. Adverse events were measured by nine studies and data for individual participants could be extracted from eight studies. This revealed that 32 of 260 (12%) patients developed a central venous catheter infection or were hospitalised because of complications related to PN.

Authors' conclusions

We are very uncertain whether HPN improves survival or quality of life in people with MBO as the certainty of evidence was very low for both outcomes. As the evidence base is limited and at high risk of bias, further higher-quality prospective studies are required.

PLAIN LANGUAGE SUMMARY

Home parenteral nutrition for people with bowel obstruction caused by cancer

What is the issue?

People with advanced cancer within the abdominal cavity can develop blockages of the bowel that cannot be treated surgically. This may cause nausea and vomiting and an inability to absorb enough nutrition via the gut. An alternative to conventional feeding when the gut does not work, is feeding through a vein, known as parenteral nutrition (PN). This is often used in hospital to support patients when return of gut function is expected. However, it can also be considered as part of palliative treatment in advanced cancer when return of gut function is unlikely.

Why is it important?

PN in people with blockage of the bowel due to advanced, inoperable cancer is controversial. Treatments are largely limited to best supportive care and there are arguments for and against artificial feeding in this situation. There is some evidence that it may lengthen survival, but the treatment can be burdensome and risky for individuals where quality of life is a priority.

We asked:

Is PN effective in improving survival and quality of life in people with inoperable blockage of the bowel caused by advanced cancer?

We found:

The benefits of PN are uncertain as the evidence is of very low certainty, provided mainly by studies that only looked at people who received PN rather than comparing patients who received PN with those who did not. As we found no randomised controlled trials, we have included the results from 13 observational studies with a total of 721 participants. For 12 of the studies, there was only one relevant treatment group and no control group. Therefore, the results are only for people receiving PN and we have no information about those not receiving it. The average survival time for people on PN varied from three to 1278 days. Only three studies measured quality of life using a recognised measure. One study found quality of life improved and two studies found similar numbers of people both improved and deteriorated. However, the three studies monitored quality of life at different points in time and measured it in different ways. Side effects occurred in 12% of people in the eight studies that measured them.

This means:

Further research is needed to find out if PN is of benefit to people with an inoperable blockage of the bowel caused by advanced cancer.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Home parenteral nutrition for people with inoperable bowel cancer

Patient or population: people with advanced cancer with inoperable malignant bowel obstruction (MBO)
Setting: outpatient/home care
Intervention: parenteral nutrition (PN)

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Length of Survival	We are uncertain whether PN improves survival for patients with MBO receiving PN. It was not possible to combine data due to heterogeneity of cancer diagnosis and differing starting points for measuring survival.There was a wide variation of survival lengths reported in the studies, with median survival periods of 15 to 155 days (range 3 to 1278 days) and mean survival intervals of 85 to 164 days (range 8 to 1004 days)	721 (13 observational studies)	⊕◯◯◯ Very Low [12]
Quality of life	We are very uncertain if PN proves quality of life for patients with MBO receiving PN. Three studies used validated questionnaires. One of these studies found an improvement over three months for global quality of life. Two studies had a mixed picture; one measuring well-being at one month and one overall quality of life at two months. Around half of participants showed no change, a quarter to a fifth deteriorated and a quarter to a third improved	188 (3 observational studies)	⊕◯◯◯ Very Low [12]

Adverse events	We are very uncertain about the impact of PN on adverse events of patients in MBO as the quality of the evidence was very low. There is limited evidence about adverse events. Although nine studies reported this outcome, data for individual patients could be extracted from eight studies and 32/260 (12%) patients developed a central venous catheter infection or were hospitalised for PN complications	280 (9 observational studies)	⊕◯◯◯ Very Low [12]

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] The studies were down graded by three points as all of the studies were observational so patients were not allocated treatments at random and healthcare professionals and patients were not blinded to treatment received. Therefore, the studies are at very high risk of bias.
[2] Narrative synthesis conducted estimates not precise

BACKGROUND

Description of the condition

Malignant bowel obstruction (MBO) is caused by mechanical, vascular or neurological dysfunction of the small or large bowel (Anthony 2007; Ripamonti 2008). People with MBO experience symptoms such as nausea, vomiting, abdominal distention and pain (Mercadante 1995).

MBO occurs most often in people who have ovarian and gastrointestinal cancers. There is a wide variation in quoted incidence rates of MBO as data have been drawn from small retrospective and autopsy studies, with reported rates varying between 5% and 51% in women with ovarian cancer and 10% to 28% in people with gastrointestinal cancer (Cousins 2016). Other cancers that have been associated with MBO include bladder cancer (3% to 10%) and endometrial (womb) cancer (3% to 11%), as well as metastatic breast cancer and melanoma (Ferguson 2015).

Some people with MBO have disease that is amenable to surgical treatment on first presentation (Cousins 2016; Daniele 2015). However, people who experience recurrences of MBO are unlikely to benefit from further surgery, at which point they are deemed to have inoperable MBO (DeBernardo 2009; Mercadante 2007). Rates of survival in the literature for people with MBO range from less than a month to up to 12 months; this wide range is due to differences in patient selection and whether the MBO resolves, treatments and definitions of survival (Mercadante 1995; Porzio 2011). However, some studies have quoted an average survival of between two and three months (Hardy 1998; Laval 2000). People with inoperable MBO are managed medically using corticosteroids, antiemetics and antisecretory agents (Ferguson 2015). For people with uncontrolled vomiting, a naso-gastric tube or venting gastrostomy may be considered (Brett 1986). People with inoperable MBO are unable to maintain adequate oral intake and may benefit from parenteral nutrition (PN).

Description of the intervention

PN is the provision of macronutrients, micronutrients, electrolytes and fluid infused as an intravenous solution. Individuals are assessed for their energy, nutrient and fluid requirements and PN solutions are then tailored to these requirements (Bielawska 2017). This solution is usually administrated to a patient during the night, over 10 to 15 hours, depending on individual tolerance, nutrition and fluid requirements (Wanten 2011). Short-term PN may be initially administrated via a peripheral or central vein. However, patients receive long-term PN and home parenteral nutrition (HPN) via a central venous catheter (Lai 2016; Pittiruti 2009). This Cochrane Review will focus on such nutritional support.

How the intervention might work

In PN, nutrients and fluids are delivered to patients via the venous route. People with MBO are able to tolerate limited, if any, oral or enteral nutrition (delivery of nutrients into the gastrointestinal tract by means of a tube), and thus are unable to meet their nutritional requirements orally. PN therefore provides a method for these patients to receive nutrients and fluid that otherwise would be inaccessible to them. PN may improve survival (Brard 2006). Median survival in people with MBO who receive PN is around 80 days (Abu-Rustum 1997; Naghibi 2015). The treatment may also improve quality of life and there have been reports of symptomatic improvement after starting PN (Mercadante 1995).

Why it is important to do this review

The provision of PN in patients undergoing palliative care is somewhat controversial. There is a fundamental human right to food, which has been recognised by the United Nations (UN) (UN 1948). However, there are clinical and ethical arguments for and against the administration of PN, related to what the person wants, their symptoms and clinical evidence. There is some evidence of benefit in terms of survival, but the treatment is costly to the healthcare provider and may be burdensome for patients (Abu-Rustum 1997; Brard 2006; DiBaise 2007; Hoda 2005; Naghibi 2015; Pasanisi 2001). There is a lack of consensus on the role of PN in this patient group which is reflected in varying rates worldwide of people with active cancer receiving PN (Howard 1995; Smith 2016). In the USA, people with cancer were the largest proportion (42%) of people receiving HPN from 1985 to 1992, although current data show that people with short-bowel syndrome are now the largest group receiving HPN (Howard 2006; Winkler 2016). In Europe as a whole, cancer is the primary indication for HPN in 39% of cases, although there are variations in different European countries for example, Denmark 8%, Belgium 23%, Spain, 39% and the Netherlands 60% (Bakker 1999). In the UK, this figure is 27% of patients (Smith 2016); all centres providing HPN to patients, including those with cancer, are expected to comply with the British Intestinal Failure Alliance Position statement (British Intestinal Failure Alliance 2016) . This Cochrane Review examines the potential benefits and disadvantages of PN for people with cancer focusing on benefits, including survival, quality of life or both, and disadvantages including any adverse events that result from the treatment.

OBJECTIVES

To assess the effectiveness of home parenteral nutrition (HPN) in improving survival and quality of life in people with inoperable MBO.

METHODS

Criteria for considering studies for this review

Types of studies

Quantitative

We did not envisage identification of randomised controlled trials (RCTs) due to sparse data and therefore we included non-randomised studies,quasi-RCTs, non-randomised controlled trials, prospective and retrospective cohort studies, including single-arm studies and case series of more than five participants.
We excluded case series with less than five participants.

Qualitative

We planned to include any qualitative studies (phenomenological, ethnographic or grounded theory) that used recognised methods of qualitative data collection (interview, observation, focus group) and analysis.

Types of participants

Inclusion criteria

The participants fulfilled each of the following criteria.

- People over 16 years of age with inoperable MBO.
- Receiving PN via a central venous catheter.
- Receiving or planned to receive PN at home.
- No curative treatment: we deemed any chemotherapy or radiotherapy in this setting as palliative.

Exclusion criteria

- Bowel obstruction caused by pseudomyxoma peritonei and desmoid tumours as these tumours are slow growing and individuals have more favourable survival.
- Receiving PN through a peripheral vein.
- Receiving only intravenous fluids that lack protein and calories.
- Studies with < 70% participants receiving PN for inoperable MBO, unless we could extract data on MBO participants.

If it was unclear whether the participants met the inclusion criteria based on the published data, we contacted the study authors for further information. If we were still unable to establish if the study met the criteria, the study was excluded.

Types of interventions

Intervention

- Treatment with PN delivered through a central venous catheter.

Control

- No PN support.
- Other nutritional interventions, such as elemental diet or intravenous fluids alone.

Types of outcome measures

Primary outcomes

- Length of survival from diagnosis of MBO or, if not given, implementation of PN until death from any cause.
- Quality of life: any measure of quality of life completed by participants, carers or an independent rater. However, we gave preference to validated questionnaires, e.g. the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30).

Secondary outcomes

- Measurement of gastrointestinal symptoms e.g. nausea, vomiting, abdominal distention, diarrhoea, pain on eating using a validated questionnaire, or recorded in a dichotomous form i.e. present/absent.
- Any measure of nutritional status, such as anthropometry or validated measures e.g. subjective global assessment.
- Qualitative reports of quality of life or symptoms.
- Where multiple time points were recorded, we gave priority to baseline, one month, three months and six months observations.
- Adverse events: sepsis caused by central venous catheter infection/hospitalisation due to HPN complications (other catheter complications, fluid overload including peripheral oedema or ascites), were reported as present or absent.
- Adverse events if they occurred at any time point during the administration of PN.
- Health economic outcomes: cost of treatment, any measurement of cost-effectiveness of treatment such as quality adjusted life year.

Search methods for identification of studies

Electronic searches

We identified relevant studies by conducting searches (January 2018) of the following electronic databases.

- Cochrane Central Register of Controlled Trials (CENTRAL, 2018, Issue 1)
- Ovid MEDLINE (1946 to January 2018)
- Embase (1980 to January 2018)

We also searched Bristish Nursing Index (BNI), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science and NHS Economic Evaluation Database (NHS EED) and Health Technology Assessment (HTA) in January 2018. We conducted a generic search for malignant bowel obstruction (MBO) and parenteral nutrition (PN) which would include qualitative and quantitative studies.

We searched for any currently recruiting trials in ClinicalTrials.gov (http://clinicaltrials.gov/) and in the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) search portal (http://apps.who.int/trialsearch/). We contacted the authors of any trials found which should have completed but for which the results were not published.

The detailed search strategy for MEDLINE is in Appendix 1, Embase in Appendix 2 and CENTRAL in Appendix 3.

Searching other resources

We handsearched selected articles to identify any other relevant articles. We also found all included articles on PubMed and searched for other pertinent articles using the 'Similar articles' feature.

Data collection and analysis

We followed the guidance of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We entered data into Review Manager (RevMan 2014). Although we planned to use SPSS (version 23) (IBM corp 2015), statistical analysis was not feasible in view of the data set.

Selection of studies

We downloaded all titles and abstracts retrieved by electronic searching to EndNote and removed duplicates. Two review authors (AMS, JS, AC, SL or CT) independently examined the remaining references and excluded those studies that clearly did not meet the inclusion criteria. JS obtained copies of the full-text of potentially relevant references. Independently, two review authors (AMS and JS) assessed the eligibility of the retrieved reports/publications. We resolved any disagreement through discussion. If it was unclear whether a study met the inclusion criteria, it was discussed with a third review author (SB). We identified and excluded duplicate reports and collated multiple reports of the same study so that each study rather than each report was the unit of interest in the review. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram and a Characteristics of included studies table (Liberati 2009).

Data extraction and management

Two review authors (AMS, JS or LH) independently extracted study characteristics and outcome data from included studies using a piloted data collection form. We noted in the Characteristics of included studies table if outcome data were not reported in a usable way. We resolved disagreements by consensus and did not need to involve a third review author (SB). One author (JS) transferred data to the RevMan 5 file (RevMan 2014). We double-checked that data had been entered correctly by comparing the data presented in the systematic review with the study reports. A second review author (AMS) did a 'spot-check' to assess the accuracy of the study characteristics against the study report.

For included studies, we extracted the following data.

- Author, year of publication and journal citation (including language).
- Country.
- Setting.
- Inclusion and exclusion criteria.
- Study design, methodology.
- Source of funding.
- Study population:
    - total number enrolled;
    - age;
    - co-morbidities;
    - performance status at diagnosis of MBO;
    - cancer diagnosis including, if indicated, staging, number and sites of metastasis and treatments received;
    - any data on confounding factors which might improve a patient's symptoms of MBO such as administration of steroids, antisecretory medication or prokinetics.
- Intervention details:
    - any details of nutrition received: PN nutritional content, number of times given in a week and whether any other oral intake was recorded;
    - Primary outcomes and Secondary outcomes as detailed above.
- Comparison:
    - whether any oral intake was recorded or intravenous fluids administered;
    - Primary outcomes and Secondary outcomes as detailed above.
- Risk of bias in study (see Assessment of risk of bias in included studies section below).
- Duration of follow-up.
- We noted the time points at which outcomes were collected and reported.

We planned to extract results as follows.

- For time-to-event data (e.g. survival), we planned to extract the log of the hazard ratio [log(HR)] and its standard error (SE) from study reports. If these were not reported, we planned to estimate the log (HR) and its SE using the methods of Parmar 1998.
- For dichotomous outcomes (e.g. gastrointestinal symptoms) we planned to extract the number of participants in each treatment arm who experienced the outcome of interest and the number of participants assessed at the endpoint, in order to estimate a risk ratio (RR).
- For continuous outcomes (e.g. quality of life measures), we planned to extract the final value and standard deviation (SD) of the outcome of interest and the number of participants assessed at endpoint in each treatment arm at the end of follow-up, in order to estimate the mean difference (MD) between treatment arms and its SE.

However, it was not possible to conduct any of these analyses as most studies only had a treatment group and no control, and for the one study with a comparator insufficient details were given.

Assessment of risk of bias in included studies

We assessed and reported on the methodological risk of bias of included studies in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), which recommends the explicit reporting of the following individual elements.

- Selection bias: random sequence generation and allocation concealment.
- Performance bias: blinding of participants and personnel.
- Detection bias: blinding of outcome assessment.
- Attrition bias: incomplete outcome data, which is less than 80% reported for primary outcomes.
- Reporting bias: selective reporting of outcomes.
- Other: any other risk of bias.

We assessed the risk of bias in non-randomised controlled studies in accordance with the additional criteria below.

- Details of criteria for assignment of participants to treatments:
    - low risk of bias: yes;
    - high risk of bias: no;
    - unclear risk of bias: if no details provided.
- Comparability of treatment groups: no differences between the two groups or differences controlled for, in particular with reference to age, performance status at diagnosis of MBO, cancer diagnosis, stage, grade, metastasis:
    - low risk of bias: if at least two of these characteristics were reported and any reported differences were controlled for;
    - high risk of bias: if the two groups differed and differences were not controlled for;
    - unclear risk of bias: if fewer than two of these characteristics were reported even if there were no other differences between the groups, and other characteristics had been controlled for.

We defined the following endpoint as a subjective outcome: quality of life.
We defined the following endpoints as objective outcomes: survival and adverse events (hospitalisation due to PN)..

Measures of treatment effect

We intended to use the following measures of the effect of treatment:

- For time-to-event data, we intended to use the HR.
- For dichotomous outcomes, we planned to analyse data based on the number of events and the number of participants assessed in the intervention and comparison groups. We planned to use these to calculate the RR and 95% confidence interval (CI).
- For continuous outcomes, we planned to analyse data based on the mean, SD and number of participants assessed for both the intervention and comparison groups to calculate MD between treatment arms with a 95% CI. If the MD was reported without individual group data, we intended to use this to report the study results. If more than one study measured the same outcome using different tools, we planned to calculate the standardised mean difference (SMD) and 95% CI using the inverse variance method in RevMan 5 (RevMan 2014).

It was not possible to undertake these calculations as most studies only had a treatment group and no control, and for the one study with a comparator insufficient details were given.

Unit of analysis issues

We used participants as the unit of analysis. In the case of repeated measurements, we recorded data at one month, three months and six months.

Dealing with missing data

We contacted study authors to obtain missing data (participant, outcome or summary data). For participant data, we conducted evidence synthesis on an intention-to-treat basis. We reported on the levels of loss to follow-up and assessed this as a source of potential bias.
For missing outcome or summary data, we have not imputed missing data and we have reported any assumptions in the review.

Assessment of heterogeneity

The studies included participants with a range of primary cancers so there was substantial clinical heterogeneity between included studies therefore meta-analysis and a statistical assessment of heterogeneity were not possible. If studies had been similar enough based on consideration of primary cancer to allow pooling of data

using meta-analysis, we planned to assess the degree of heterogeneity by:

- visual inspection of forest plots;
- estimation of the percentage heterogeneity (I^2 statistic) between trials which cannot be ascribed to sampling variation (Higgins 2003);
- formal statistical test of the significance of the heterogeneity (Chi^2 test) (Deeks 2001).

We intended to regard heterogeneity to be substantial if the I^2 statistic value was greater than 30% and either the T^2 value was greater than zero, or there was a low P value (< 0.10) in the Chi^2 test for heterogeneity.
Given the heterogeneity of the data, we used a narrative approach to synthesise the data.

Assessment of reporting biases

It was not possible to explore publication bias using a funnel plot (Higgins 2011).

Data synthesis

Quantitative synthesis

We intended to perform a meta-analysis using the fixed-effect model in RevMan 5 (RevMan 2014) if a sufficient number of clinically similar studies (in terms of primary cancer diagnosis) were available to ensure meaningful conclusions, and if statistical heterogeneity was low (I^2 statistic < 30%). If there was variability in the primary cancer diagnosis of included studies, or if statistical heterogeneity was substantial (I^2 statistic > 30%), we planned to use the random-effects model with inverse variance for meta-analysis (DerSimonian 1986). We planned to only include non-randomised studies with two or more comparison groups if statistical adjustments were made for baseline imbalances.

- For time-to-event data, we planned to pool HRs using the generic inverse variance facility in RevMan 5 (RevMan 2014).
- For any dichotomous outcomes, we intended to calculate the RR for each study and we would then have pooled these.
- For continuous outcomes, we planned to pool the MD between the treatment arms at the end of follow-up, if all trials measured the outcome on the same scale; otherwise we intended to pool standard mean difference (SMD) values.

However, we were unable to pool the data statistically using meta-analysis, therefore we conducted a narrative synthesis of the results.

Qualitative synthesis

It was not possible for us to undertake a meta-synthesis as no qualitative studies were identified.

Subgroup analysis and investigation of heterogeneity

We reported on different lengths of survival of participants with different types of cancer where these data were available.

Sensitivity analysis

Insufficient numbers of studies met the review inclusion criteria to undertake a sensitivity analysis to determine if the findings were altered by excluding trials of high risk of bias as determined by the Cochrane 'Risk of bias' tool (Higgins 2011).
We did not find any qualitative studies, therefore assessing whether any one article was adding disproportionately to the findings was not required.

'Summary of findings' table

To interpret the findings and to rate the certainty of the evidence, two review authors (AMS and JS) used the GRADE approach (Guyatt 2011) and the guidelines provided in Chapter 12.2 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2011). First, we analysed the overall certainty of evidence for each outcome individually, downgrading the evidence from 'low' as all the studies were observational to 'very low' depending on the risk of bias, indirectness of evidence, inconsistency, imprecision of effect estimates or potential publication bias. Afterwards, we took this into account to draft the review conclusions. We used the GRADEpro GDT software to produce a 'Summary of findings' table with the results of this analysis (GRADEpro 2015). We considered the following outcomes.

- Survival.
- Quality of life measured on a validated questionnaire.
- Adverse events of central venous catheter infection or hospitalisation due to PN.

Meta-analysis was not possible, so we have presented results in a narrative 'Summary of findings' table format, such as that used by Chan 2011 (Summary of findings for the main comparison).

RESULTS

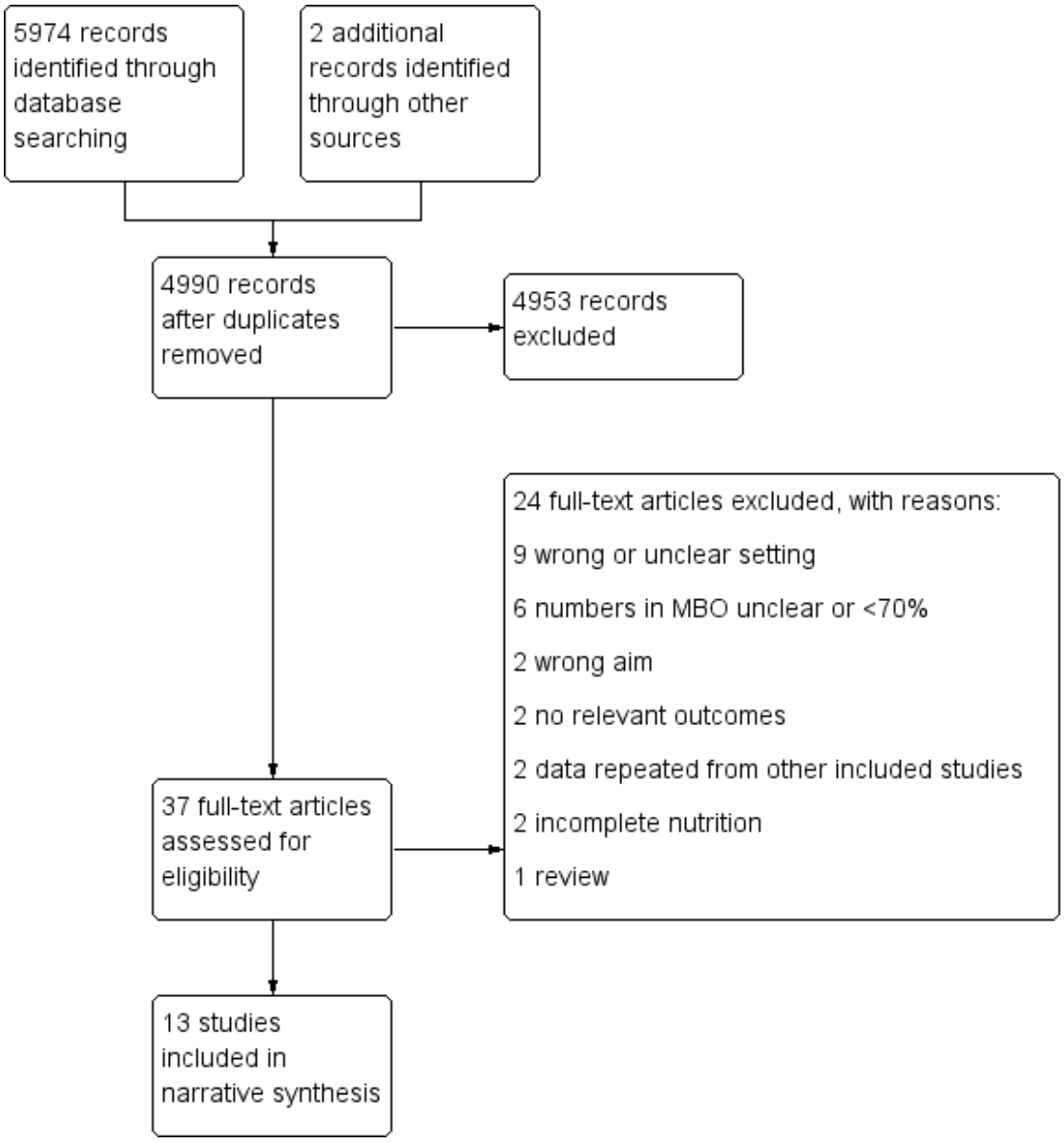
Description of studies

Results of the search

Combining the references and removing the duplicates produced a list of 3114 references. We conducted further electronic searches on BNI, CINAHL, Web of Science, NHS Economic Evaluation, Health Technology Assessment, ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform. This uncovered a further 2120, which was reduced

to 1876 once duplicates were removed. The resulting 4990 references were screened for relevance by two review authors. The following authors screened studies: AMS, JS, CT, AC and SL. This identified 146 references that were potentially eligible for inclusion in the review. Two review authors(AMS and JS) excluded 111 studies as not meeting the inclusion criteria on full-text review; one study which should have completed could not be found in full text and we had no response from the contact author,further details can be found in Characteristics of ongoing studies. We excluded a further 24 studies following discussion with a third review author (SB). Two additional references were found; one from using the similar articles feature on Pubmed and one from screening the reference lists of other studies. A total of 13 studies with a total of 721 participants were included in the review.
For further details, please see the PRISMA diagram Figure 1

Figure 1. Study flow diagram.



Included studies

See Characteristics of included studies

Design

We included 13 studies in the review. Six studies were conducted prospectively (Bozzetti 2002; Chermesh 2011; Cotogni 2017; Finocchiaro 2002; Mercadante 1995; Pironi 1997), and seven retrospectively (Abu-Rustum 1997; August 1991; Duerksen 2004; Keane 2018; King 1993; Santarpia 2006; Soo 2008). From the prospective studies two were cohort (Chermesh 2011; Cotogni 2017) and four were case series (Bozzetti 2002; Finocchiaro 2002; Mercadante 1995; Pironi 1997) and from the retrospective studies, six were case series (August 1991; Duerksen 2004; Keane 2018; King 1993; Santarpia 2006; Soo 2008), and one was a cohort study (Abu-Rustum 1997). We contacted the authors of three included studies for more information on patient characteristics and received no further data from them (Abu-Rustum 1997; Bozzetti 2002; Pironi 1997).

Setting

Three included studies were conducted in the USA (Abu-Rustum 1997; August 1991; King 1993), six in Italy (Bozzetti 2002; Cotogni 2017; Finocchiaro 2002; Mercadante 1995; Pironi 1997; Santarpia 2006), one in Israel (Chermesh 2011), one in Canada (Soo 2008), and one in England (Keane 2018). All the participants had parenteral nutrition (PN) at home. One study included participants who had PN in hospital and at home (Duerksen 2004), however, data were only extracted for participants at home.

Participants

There were 721 participants considered in this review of which 308 were male and 384 female. We were unable to extract the gender for 29 participants. There was a wide age range; some studies gave age as median which varied between 54 to 62 years (range 32 to 79 years) and others as mean 48.76 (SD 13.8) to 60 (SD 28) years.
There was a wide variety of cancer diagnoses in participants: 237 gynaecological (including ovarian, endometrial, cervical and peritoneal), 390 gastro-intestinal (oesophagus, stomach, pancreas, colorectal and appendix), 14 lung,11 breast, five haematological, four kidney, three head-neck, and 57 from other sites.
Some of the participants received oncology treatment whilst on PN; 174 had chemotherapy, 20 had radiotherapy and 14 had surgery, with some participants receiving more than one treatment (Abu-Rustum 1997; Bozzetti 2002; Cotogni 2017; King 1993; Soo 2008). Five studies gave no details about whether participants were receiving any treatment (August 1991; Chermesh 2011; Mercadante 1995; Pironi 1997; Santarpia 2006). In one study, chemotherapy was given to some participants, but it is unclear whether this pertained to the participants included in this review (Duerksen 2004), and in two other studies the numbers receiving chemotherapy whilst on PN were unclear (Finocchiaro 2002; Keane 2018).
In most of the studies, there was no information about the oral intake of the participants (August 1991; Bozzetti 2002; Chermesh 2011; Duerksen 2004; Keane 2018; King 1993; Mercadante 1995; Pironi 1997; Santarpia 2006; Soo 2008). Finocchiaro 2002 reported that 32 participants (46%) were taking oral nutrition, but gave no information as to calorie intake, and similarly. Abu-Rustum 1997 commented that participants were taking a liquid diet, but gave no information on oral energy intake. Cotogni 2017 reported participants taking a median of 500 kcal per day.
Baseline performance status was measured and reported in nine studies using Karnofsky performance status, where a higher score indicates better performance (Bozzetti 2002; Cotogni 2017; Duerksen 2004; Finocchiaro 2002; Keane 2018; King 1993; Pironi 1997; Santarpia 2006; Soo 2008). Four studies reported median Karnofsky performance status, which was 60 to 70 (range 40 to 90) (Bozzetti 2002; Cotogni 2017; Duerksen 2004; Finocchiaro 2002). Keane 2018 and Soo 2008 reported mean Karnofsky performance status as 50 ± 16 and 62.7 (SD 18.52), respectively. King 1993 reported Karnofsky performance status as 48, but it was unclear if this was mean or median and no range or standard deviation *SD) was given. Pironi 1997 found Karnofsky performance status was 30 to 40 in 9 (31%) participants, 50 to 60 in 18 (62%) participants and 70 to 80 in 2 (7%) participants. Santarpia 2006 reported Karnofsky performance status as $\leq$ 40 in 12 participants and $\geq$ 50 in 52 participants. No measure of performance status was reported in four studies (Abu-Rustum 1997; August 1991; Mercadante 1995; Chermesh 2011)
No studies reported on confounding factors such as use of steroids, which may improve the symptoms of malignant bowel obstruction (MBO); neither did any studies comment on co-morbidities in participants.

Interventions

The intervention we considered was home parenteral nutrition (HPN) and all of the participants identified in included studies received PN at home. However, six of the studies gave no details about the nutritional composition of administrated solutions (Abu-Rustum 1997; Chermesh 2011; Cotogni 2017; Duerksen 2004; King 1993; Pironi 1997), whereas this information was available in the other studies.
In August 1991, solutions contained 1.0 L to 3.0 L of crystalline amino acid (4.25% or 5.0%), dextrose (25% to 35%), and ap-

propriate electrolytes, vitamins and minerals. Most participants received lipid emulsion (250 mL of a 20% solution) weekly. Participants had individually-tailored regimens, although no details were given. In Bozzetti 2002, the aim was 30 non-protein kcal/kg/day for participants. The median values for the PN preparations were 300 g/day glucose (range 160 g to 500 g), 60 g/day lipid (range 42 g to 100 g) and 12 g/day nitrogen (range 6.2 g to 13.7 g). Finocchiaro 2002 aimed to match energy intake with nutritional guidelines for the Italian population multiplied by a specific illness factor (Società Italiana Nutrizione Umana 1996), 1.2 g/kg/day protein and 30 mL to 35 mL/kg/day fluid. Initially, participants were given 1500 mL/day (750 mL to 2500 mL), 1400 kcal/day (600 kcal to 1900 kcal), 60 g/day (30 g to 85 g) of protein and added micronutrients, which gave them 27.8 mL/kg (13.3 mL to 52.6 mL) and 24.4 kcal/kg (8.5 kcal to 40 kcal). In Mercadante 1995, solutions contained 1500 kcal to 2000 kcal, composed of dextrose (providing 60% to 70% of energy) and 10% fat emulsion (approximately 30% to 40% energy), essential amino acids enriched with branched-chain L-amino acids (approximately 17 g to 20 g), and electrolytes and vitamins as required. Keane 2018 gave mean requirements for PN, which were volume 2251 mL ± 626 mL, 11 ± 3 g/day nitrogen, 911 ± 304 kcal/day glucose, 573 ± 262 kcal/day lipid, 112 ± mmol/day sodium, 57 ± 26 mmol/day potassium, 5 ± 2 mmol/day calcium, 10 ± 5 mmol/day magnesium and 21 ±10 mmol/day phosphate. Santarpia 2006 did not comment on solution composition, but aimed for individualised nutritional support providing 20 to 30 kcal/kg/day, 3 to 4 g/kg/day carbohydrate, 1 g/kg/day lipid and 1.0 to 1.5 g/kg/ day protein. Similarly, Soo 2008 did not comment on solution composition, but aimed for 25 kcal/kg, 1 g/kg protein and standard provision of micronutrients for participants.

Comparators

Ten studies were case series that lacked comparator arms (August 1991; Bozzetti 2002; Duerksen 2004; Finocchiaro 2002; Keane 2018; King 1993; Mercadante 1995; Pironi 1997; Santarpia 2006; Soo 2008). One study (Abu-Rustum 1997) compared chemotherapy and PN with chemotherapy alone and another (Cotogni 2017) compared PN and treatment (chemotherapy, radiotherapy or a combination of both) with PN alone. One study had a comparator that was not relevant for this review (Chermesh 2011), which compared PN in MBO with benign disease. However, data were only extracted for the MBO participants.

Outcome

Survival

All of the studies reported the overall survival of participants on PN. However, the definition of survival was inconsistent between the studies, and at times unclear. Some defined survival from the start of HPN (Bozzetti 2002; King 1993; Santarpia 2006), which could be assumed to be from discharge, until death. Other studies explicitly stated that survival was measured from discharge until death (August 1991; Chermesh 2011; Keane 2018); whilst others were unclear, but it has been assumed by the review authors that the survival interval was calculated from discharge until death (Cotogni 2017; Finocchiaro 2002; Pironi 1997; Soo 2008). Abu-Rustum 1997 measured survival from venting gastrostomy placement. In Mercadante 1995 and Duerksen 2004, survival was measured from initiation of PN. Therefore, in these three studies (Abu-Rustum 1997; Duerksen 2004; Mercadante 1995), survival was calculated over a longer time period as the measurement started whilst the patient was in hospital.

Quality of life

Four of the studies described quality of life of participants receiving HPN (Bozzetti 2002; Cotogni 2017; Finocchiaro 2002; King 1993). Three of the studies used a validated instrument to measure quality of life (Bozzetti 2002; Cotogni 2017; Finocchiaro 2002): Bozzetti 2002 used the Rotterdam Symptom Checklist, which participants filled in monthly, and presented detailed results from 64 participants after one month on PN; lower scores represent better quality of life. Cotogni 2017 used participant-completed European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 Version 3.0 (EORTC QLQ-C30). Scores ranged between zero and 100 with higher scores indicating better quality of life in the domains: global quality of life, physical functioning, role functioning, emotional functioning, cognitive functioning and social functioning. In the domains: appetite loss, fatigue, nausea and vomiting and financial impact, lower scores indicate a better quality of life. Participants completed the questionnaire before initiation of HPN in the presence of a healthcare professional and subsequently at home, monthly for four months. Finocchiaro 2002 used the Therapy Impact Questionnaire with 27 participants treated for more than two months, although it was unclear who completed the questionnaire; lower scores indicated a better quality of life. King 1993 employed various criteria to assess quality of life. Physical and psychological well-being were assessed by Karnofsky Performance Status, level of activity, morale and presence of pain, fatigue, gastrointestinal discomfort, nausea, vomiting and diarrhoea; apart from Karnofsky Performance Status, criteria were measured by a one (usual or best) to five (worse or never) scale. Social interactions with friends and family were also measured on the same one-to-five scale. King 1993 also reported participant employment or recreational travel as present or absent. It was unclear in the King 1993 study who was assessing participant quality of life, but they gathered the information from medical records, interviews with participants and family, and from healthcare professionals.

Measurement of gastrointestinal symptoms

Most studies did not monitor gastrointestinal symptoms. However in some studies gastrointestinal symptoms were measured in combination with other symptoms and could not be abstracted separately (Bozzetti 2002; Cotogni 2017). King 1993 investigated gastrointestinal discomfort, nausea and vomiting and diarrhoea using a scale of one (usual or best) to five (worst or never) prior to PN and at one-month intervals. Finocchiaro 2002 presented symptoms of nausea and vomiting in 27 participants treated for longer than two months on HPN; these were measured as part of the Therapy Impact Questionnaire where a lower score indicates a better outcome.

Measurement of nutritional status

Four studies (Bozzetti 2002; Finocchiaro 2002; King 1993; Santarpia 2006) measured nutritional status. Bozzetti 2002 monitored nutritional status at the start of treatment until death; measuring weight, serum albumin, lymphocyte count and serum transferrin. Finocchiaro 2002 reported on nutritional status before PN and after two months in the 27 (of 70 participants) who survived longer than two months. They measured weight and patient-generated-subjective global assessment (PG-SGA); PG-SGA is measured as either A, B or C with A representing the best nutritional status and C the worst. King 1993 measured nutritional status prior to HPN and at one week, one month, three months, six months and one year; as per protocol we report on measures at baseline, one month, three months and six months. King 1993 measured weight, serum albumin and serum transferrin. Santarpia 2006 reported weight at baseline and one month in two tables for participants who lived more than 60 or 90 days. We report the data for 64 participants surviving for 60 or more days.

Qualitative reports of symptoms

No studies had qualitative reports of symptoms.

Adverse events

Nine studies gave information on adverse events (August 1991; Chermesh 2011; Cotogni 2017; Duerksen 2004; Finocchiaro 2002; King 1993; Mercadante 1995; Pironi 1997; Soo 2008). They included information about a variety of major and minor adverse events that participants encountered, but as per protocol, we report only on central venous catheter infection and hospitalisations due to PN complications.

Health economic outcomes

Two of the studies considered cost (Mercadante 1995; Pironi 1997). However, they did not consider cost in a health economic evaluation such as quality adjusted life years.

Excluded studies

See Excluded studies

We provide details of 24 excluded studies. We listed studies as excluded if they were obtained in full text and were discussed by three review authors: AMS, JS and SB. The summary of reasons for exclusion included the following.

- The study did not address the aim of the review (Bozzetti 2015; Chen 2013; Diver 2013; Villares 2001; Villares 2004).
- Patients did not received HPN (Brard 2006; Chakraborty 2011; Chouhan 2016; Fan 2007; Oh 2014; Szefel 2016; Tunca 1981).
- The number of people with MBO was not specified or was lower than 70% (Bozzetti 2014; Girke 2016; Hoda 2005; Mercadante 2015; Tang 1995; Vashi 2014).
- Only hydration was received by patients (Gemlo 1986; Mercadante 1995a).
- Data were included in another study (Pasanisi 2001;Gupta 2015).
- Review article (Naghibi 2015).
- Unable to extract data from patients who received home parenteral nutrition Guerra 2015.

Risk of bias in included studies

All the studies were case series or cohort studies; participants were not randomised to treatments, there was no group allocation concealment and no blinding of participants, personnel or assessors. Therefore, the risk of bias in all studies was high.

Allocation

Allocation bias was high in all studies. Participants were not randomised to treatments and there was no group allocation concealment. In most of the studies there was only one treatment group and no comparator (August 1991; Bozzetti 2002; Duerksen 2004; Finocchiaro 2002; Keane 2018; King 1993; Mercadante 1995; Pironi 1997; Santarpia 2006; Soo 2008). Three studies had two groups (Abu-Rustum 1997; Chermesh 2011; Cotogni 2017); although Chermesh 2011 compared participants with MBO and those with benign disease and only MBO participants are included in this review. The decision for which treatments a participant received seems to have been clinically driven as no information is given about group allocation.

Blinding

Performance and detection bias for all studies is high as there was no blinding of participants, healthcare professionals or assessors to treatment received.

Incomplete outcome data

Attrition bias across most of the studies was low as all participants were accounted for in the outcomes measured (Abu-Rustum 1997; August 1991; Bozzetti 2002; Chermesh 2011; Duerksen 2004; Keane 2018; Mercadante 1995; Pironi 1997; Santarpia 2006; Soo 2008). In four studies there was a high attrition rate in the measurement of quality of life or nutritional status due to patient death (Cotogni 2017; Finocchiaro 2002; King 1993; Santarpia 2006). In Cotogni 2017, quality of life was measured at four months in less than half the participants. Finocchiaro 2002 only measured quality of life and nutritional status in 27 of 70 participants who had PN for longer than four months. In King 1993, there was a high attrition rate in measurement of nutritional status with only 18 out of 61 participants measured at three months. Santarpia 2006 measured nutritional status at one month in those surviving more than 60 days in 64 of 152 participants.

Selective reporting

It was unclear if selective reporting was present as we were unable to locate protocols for the studies.

Other potential sources of bias

There did not appear to be any other sources of bias present.
The risk of bias in the included studies is summarised in Figure 2 and displayed graphically in Figure 3

Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

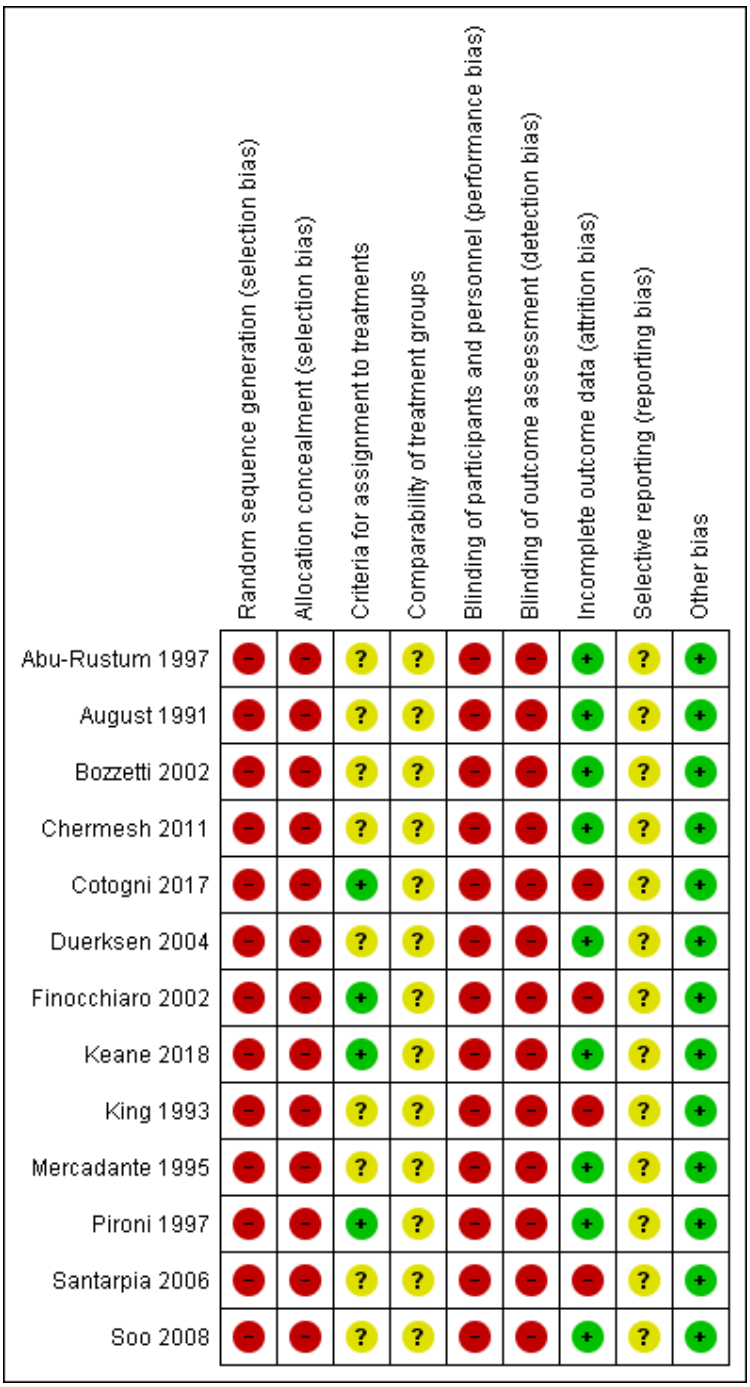
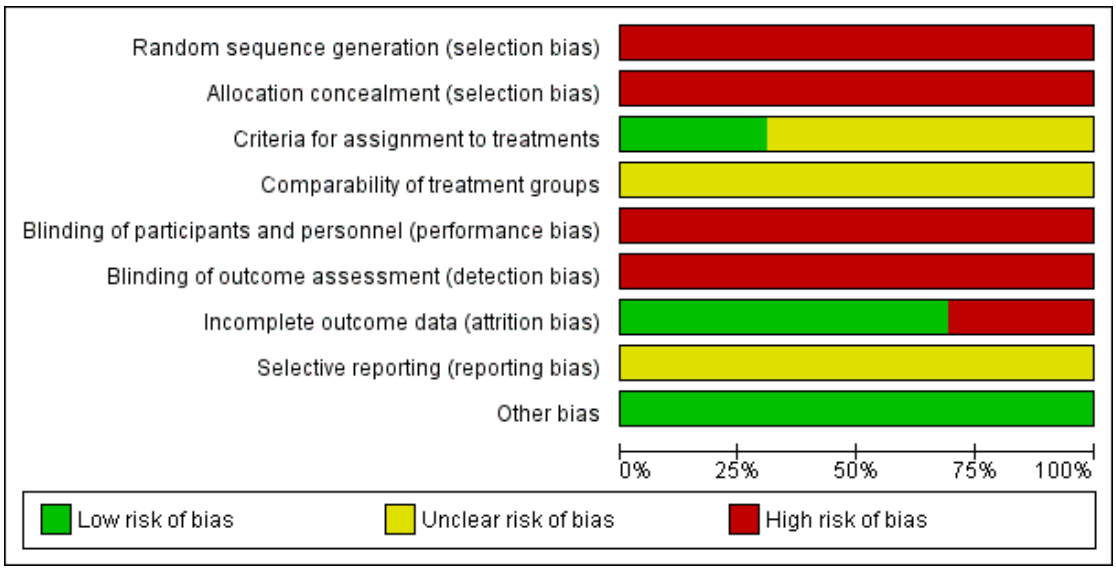


Figure 3. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Effects of interventions

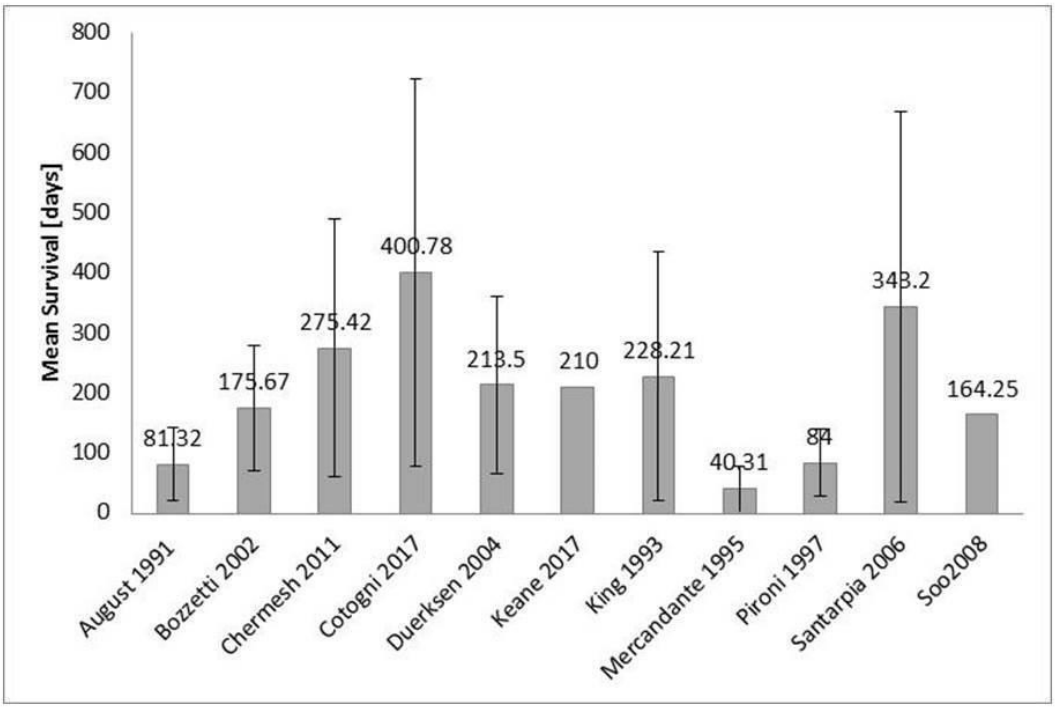
See: **Summary of findings for the main comparison** Parenteral nutrition (PN) for inoperable malignant bowel obstruction (MBO)

Primary outcomes

Survival

Survival was measured in all of the studies; see Figure 4. Seven of the studies (August 1991; Chermesh 2011; Cotogni 2017; Duerksen 2004; Keane 2018; Mercadante 1995; Santarpia 2006) gave survival at different time points, as can be seen in Table 1. However, we are uncertain whether HPN improves survival in MBO patients as the evidence was very low certainty.

Figure 4. Mean survival and standard deviations calculated from median and range (Hozo 2005) for all studies apart from Keane 2018; Pironi 1997; Soo 2008 which presented mean survival



In six of the studies, all of the participants had MBO (Abu-Rustum 1997; August 1991; Chermesh 2011; Duerksen 2004; Mercadante 1995; Santarpia 2006). The median survival of participants across the studies was 15 days to 155 days with a range of three days to 1278 days.

However, in seven of the studies the percentage of participants with MBO ranged from 70% to 89% (Bozzetti 2002; Cotogni 2017; Finocchiaro 2002; Keane 2018; King 1993; Pironi 1997; Soo 2008); the other participants in the group were given PN for other reasons such as poor oral intake. The median survivals intervals were two to four months with a range of 0.07 to 26 months. Keane 2018, Pironi 1997 and Soo 2008 calculated survival as arithmetic means rather than medians and found a mean survival of 12 (SD 8) weeks and five months (range 0.25 to 33), respectively. Keane 2018 reported both median survival, 14 weeks (interquartile range (IQR) 5 to 34), and mean survival 31 weeks (95% CI 21 to 40). Finocchiaro 2002 did not report mean or median survival, but at the end of the 14-month study period 41 out of 70 participants had died.

There were no patients lost to follow up from any of the studies.

In five studies (Abu-Rustum 1997; August 1991; Duerksen 2004; Mercadante 1995; Santarpia 2006), all patients had died by the end of the study period. Five studies clearly stated the number of patients alive at the end of the study (Chermesh 2011; Cotogni 2017; King 1993; Pironi 1997; Soo 2008); the numbers alive ranged from one to 13 patients, which was between 3% to 12% of the study populations. In Bozzetti 2002; Finocchiaro 2002 and Keane 2018, it was unclear how many patients were still alive at the end of the study period as all had patients censored from the analysis; for example if patients resumed oral intake or refused HPN.

In addition to investigating overall survival, Abu-Rustum 1997 investigated survival in participants treated with chemotherapy and PN and participants treated with chemotherapy alone; median survival was 89 days and 71 days, respectively. In contrast, Cotogni 2017 measured survival in 72 participants receiving PN and treatment (chemotherapy, radiotherapy or both) and in 39 participants receiving only PN; after three months, 54 (75%) participants with treatment survived compared to 20 (51%) partici-

pants with no treatment; after six months, 10 (26%) participants with no treatment survived compared to 28 (39%) participants having treatment.

Two of the studies described survival statistics according to the different primary cancer diagnoses (August 1991; Duerksen 2004); see Table 2. Ovarian cancer had the shortest median survival and gastric cancer had the longest.

Quality of life

Quality of life was measured by four studies (measured in 268 participants) (Bozzetti 2002; Cotogni 2017; Finocchiaro 2002; King 1993). We are uncertain whether HPN improves quality of life in MBO patients as the evidence was very low certainty. The studies using a validated measure (Bozzetti 2002; Cotogni 2017; Finocchiaro 2002) presented a mixed picture. Cotogni 2017 found an improvement over three months for global quality of life. Two studies (Bozzetti 2002; Finocchiaro 2002), reported around half of participants showed no change, a quarter to a fifth deteriorated and a quarter to a third improved.

More information about quality of life for the three studies with validated measures (Bozzetti 2002; Cotogni 2017; Finocchiaro 2002) is given in Table 3

Secondary outcomes

Measurement of gastrointestinal symptoms

Two studies (measured in 88 participants) (Finocchiaro 2002; King 1993) measured gastrointestinal symptoms and found some participants symptoms improved, others deteriorated and some had no change; see Table 4. We are uncertain whether HPN improves gastrointestinal symptoms in MBO patients as the evidence was very low certainty.

Measurement of nutritional status

Four studies (measured in 221 participants) (Bozzetti 2002; Finocchiaro 2002; King 1993; Santarpia 2006), measured nutritional status and found that it was maintained. However, we are uncertain of the impact of HPN on nutritional status as the evidence was very low certainty.

More information about nutritional status is given in Table 5

Qualitative reports of symptoms

No studies contained qualitative descriptions of symptoms.

Adverse events

Nine studies (371 participants) gave information on adverse events (August 1991; Chermesh 2011; Cotogni 2017; Duerksen 2004; Finocchiaro 2002; King 1993; Mercadante 1995; Pironi 1997; Soo 2008); see Table 6 for more details. Eight studies (August 1991; Chermesh 2011; Duerksen 2004; Finocchiaro 2002; King 1993; Mercadante 1995; Pironi 1997; Soo 2008) reported the number of participants with adverse events and 32 of 280 participants had a central venous catheter infection or were hospitalised for PN complications, which equated to between 6% and 21% of participants across the studies. Cotogni 2017 reported complications in the standardised way and found 0.33 catheter-related bloodstream infections per 1000 catheter days. However, this reporting differed from the other studies and it is unclear how many participants this relates to. Although not specified in all studies, it was assumed that any patients with central venous catheter infections were hospitalised. The Common Terminology Criteria for Adverse Events considers any hospitalisation as a grade three or severe complication (US Department of Health and Human Services, 2017).

The other studies did not report adverse events. It was not clear whether this was because participants did not suffer from any or they were not reported.

Health economic outcomes

Two studies (42 participants) considered cost (Mercadante 1995; Pironi 1997). Mercadante 1995 considered the cost of providing PN solution, which in 1995 was $80 daily. However, this figure does not include pharmacist time or other healthcare costs. Pironi 1997 found that in from 1 July 1995 to 30 June 1996, the cost of the nutrition support team was approximately 14.2 European Currency Units for each patient per day and 61 European Currency Units for solutions, lines and dressing kits.

For an overview of the findings, see Summary of findings for the main comparison.

DISCUSSION

Summary of main results

This review included 721 participants from 13 studies (Abu-Rustum 1997; August 1991; Bozzetti 2002; Chermesh 2011; Cotogni 2017; Duerksen 2004; Finocchiaro 2002; Keane 2018; King 1993; Mercadante 1995; Pironi 1997; Santarpia 2006; Soo 2008). No randomised controlled trials were identified and 10 studies had a single arm without a comparator group (August 1991; Bozzetti 2002; Duerksen 2004; Finocchiaro 2002; Keane 2018; King 1993; Mercadante 1995; Pironi 1997; Santarpia 2006; Soo 2008). However, conducting randomised controlled trials in this area is ethically difficult as patients who are not eating would be allocated to being fed on a random basis.

Survival

We are very uncertain about the impact of parenteral nutrition (PN on survival of patients with malignant bowel obstruction (MBO) as the certainty of the evidence was very low. Survival was reported in all of the studies and 636 or 88% of participants were dead at the end of the study and included in the survival analysis (Abu-Rustum 1997; August 1991; Bozzetti 2002; Chermesh 2011; Cotogni 2017; Duerksen 2004; Finocchiaro 2002; Keane 2018; King 1993; Mercadante 1995; Pironi 1997; Santarpia 2006; Soo 2008). There was a wide variation of survival intervals reported in the studies, with median survival periods of 15 to 155 days (range three to 1278 days) and mean survival intervals of 85 to 164 days (range eight to 1004 days). Unfortunately, due to heterogeneity of cancer diagnosis and the differing start points for measuring survival it was not possible to combine the study results. Although, the hospital discharge date was most often used as the start point for measuring survival, this is relatively arbitrary and influenced by many non-disease-related factors making comparisons across hospitals and different health systems difficult.

Quality of life

We are very uncertain about the impact of PN on quality of life of patients with MBO as the certainty of the evidence was very low. Results for quality of life were equivocal. Three studies used validated questionnaires (Bozzetti 2002; Cotogni 2017; Finocchiaro 2002). Cotogni 2017 found an improvement over three months for global quality of life. Bozzetti 2002 and Finocchiaro 2002 had a mixed picture showing both improvements for some patients and deterioration for others

Adverse events

We are very uncertain about the impact of PN on adverse events of patients with MBO as the certainty of the evidence was very low. Adverse events were reported in nine studies (August 1991; Chermesh 2011; Cotogni 2017; Duerksen 2004; Finocchiaro 2002; King 1993; Mercadante 1995; Pironi 1997; Soo 2008). For eight studies, data for individual participants could be extracted, and 32 of 260 (12%) participants developed a central venous catheter infection or were hospitalised for PN complications (August 1991; Chermesh 2011; Duerksen 2004; Finocchiaro 2002; King 1993; Mercadante 1995; Pironi 1997; Soo 2008).

Overall completeness and applicability of evidence

The applicability and generalisability of the evidence for parenteral nutrition in MBO is limited due to lack of adequate and comparative data across the studies.

All of the studies reported survival data in some way, but there were flaws in the estimates in terms of start point.
Quality of life was only measured in four studies and sequential measurements were limited due to participant mortality.
Adverse events were only reported in nine of the 13 studies. It was unclear whether no adverse events occurred in the other studies or whether they were just not reported.

Quality of the evidence

Overall, the certainty of evidence was very low, derived mainly from observational studies without a comparator.

Potential biases in the review process

The main bias is that evidence comes from case series and cohort studies. There was no randomisation to treatment groups and no blinding of participants or healthcare professionals. The measurement of survival in 10 of the included studies was unclear or flawed in that a process measure (discharge date) was used to define the start point for measuring survival (August 1991; Bozzetti 2002; Chermesh 2011; Cotogni 2017; Finocchiaro 2002; Keane 2018; King 1993; Pironi 1997; Santarpia 2006; Soo 2008).

Agreements and disagreements with other studies or reviews

Naghibi 2015 conducted a systematic review of people with MBO having PN. They included 12 studies where more than 80% of the participants had MBO. the study authors reported a survival time of 83 days (median) and 116 days (mean). Unlike Naghibi 2015, we did not perform a meta-analysis of the survival time due to the variety of cancer diagnoses, differing definitions of survival time and flawed definition of survival period. However, there was a range median survivals across the studies 15 to 155 days (range three to 1278 days), which is comparable to that reported by Naghibi 2015 (median survivals were 15 to 140 days with a range of three to 1004 days). Similar to our findings, Naghibi 2015 found limited data on quality of life and suggested that further research into quality of life in these participants is required.
Naghibi 2015 also conducted base-case economic modelling for HPN in palliative malignancy and found an incremental cost-effectiveness ratio of £176, 587 per quality adjusted life year. None of the studies in this review conducted quality adjusted life year cost analysis of HPN.

AUTHORS' CONCLUSIONS

Implications for practice

Due to the very low certainty of evidence, we are very uncertain whether parenteral nutrition (PN) improves length and quality of life in people with malignant bowel obstruction (MBO).

Implications for research

The certainty of evidence in this review is very low and well-designed prospective research is required. This is an area where it is considered ethically difficult to conduct randomised controlled trials, as noted above. However, it might be possible to randomise people with very short estimated survival intervals to simple intravenous fluid support (e.g. saline) or parenteral nutrition (PN).

The majority of studies in this review were based on data from one centre and there was heterogeneity in the cancer diagnosis, and across the studies, in definitions of outcome measures. In order to gather sufficient data to answer the question regarding the impact of PN on survival and quality of life in MBO, prospective national or international cohort studies are required with centres working to the same protocol. Although, historically practice in the UK and other countries (e.g. Denmark) has differed from the practice in some countries such as USA and Italy in terms of percentage of patients receiving PN with advanced cancer, the UK has seen an increase use of PN in cases with advanced cancer (Brandt 2017; Dibb 2017). Moreover, working from the same protocol would mitigate against differences across countries. To give a robust measure, survival could be measured from the time PN commences in addition to the time of discharge home. Investigation of quality of life would benefit from qualitative studies using robust methods, and quantitatively, the use of validated patient-reported outcome measures and validated quality of life questionnaires (Aaronson 1993; Wilburn 2017). It may be useful to investigate change in quality of life relative to baseline over the whole time period on PN, as it could produce an initial improvement which falls with advancing disease. In addition to investigating survival, there is a need to be able to assess prognosis in people with MBO. It could be argued that PN is adds little to patient survival if they succumb to their disease within two weeks of starting the treatment. However, most people could not survive without nutrition for more than 12 weeks and PN would seem beneficial in this instance. Currently, guidelines for the use of HPN are based on predicting survival (Bozzetti 2009). There is an urgent need to develop assessment tools to estimate prognosis in these patients to enable HPN to be offered to patients who are likely to live beyond the time required to organise home parenteral nutrition (HPN).

ACKNOWLEDGEMENTS

We thank Jo Morrison for clinical and editorial advice; and Gail Quinn, Clare Jess and Tracey Harrison for their contributions to the editorial process. Also we are grateful to Jo Platt for designing and executing the search strategy.

This project was supported by the National Institute for Health Research (NIHR), via Cochrane infrastructure funding to the Cochrane Gynaecological, Neuro-oncology and Orphan Cancers Group. The views and opinions expressed therein are those of the review authors and do not necessarily reflect those of the Systematic Reviews Programme, the NIHR, the NHS or the Department of Health.

We would like to thank the referees for many helpful suggestions and comments, some of these include Kathie Godfrey, Sonali Kaushik and Agnieszka Michael.

REFERENCES

References to studies included in this review

Abu-Rustum 1997 *{published data only}*
Abu-Rustum NR, Barakat RR, Venkatraman E, Spriggs D. Chemotherapy and total parenteral nutrition for advanced ovarian cancer with bowel obstruction. *Gynecologic Oncology* 1997;**64**:493–5.

August 1991 *{published data only}*
August DA, Thorn D, Fisher RL, Welchek CM. Home parenteral nutrition for patients with inoperable malignant bowel obstruction. *Journal of Parenteral and Enteral Nutrition* 1991;**15**:323–7.

Bozzetti 2002 *{published data only}*
Bozzetti F, Cozzaglio L, Biganzoli E, Chiavenna G, De Cicco M, Donati D, et al. Quality of life and length of survival in advanced cancer patients on home parenteral nutrition. *Clinical Nutrition* 2002;**21**:281–8.

Chermesh 2011 *{published data only}*
Chermesh I, Mashiach T, Amit A, Haim N, Papier I, Efergan R, et al. Home parenteral nutrition (HTPN) for incurable patients with cancer with gastrointestinal obstruction: do the benefits outweigh the risks?. *Medical Oncology* 2011;**28**:83–8.

Cotogni 2017 *{published data only}*
Cotogni P, De Carli L, Passera R, Amerio ML, Agnello E, Fadda M, et al. Longitudinal study of quality of life in advanced cancer patients on home parenteral nutrition. *Cancer Medicine* 2017;**6**:1799–806.

Duerksen 2004 *{published data only}*
Duerksen DR, Ting E, Thomson P, McCurdy K, Linscer J, Larsen-Celhar S, et al. Is there a role for TPN in terminally ill patients with bowel obstruction?. *Nutrition* 2004;**20**:760–3.

Finocchiaro 2002 *{published data only}*
Finocchiaro C, Gervasio S, Agnello E, Appiano S, Bertetto O, Ciuffreda L, et al. Multicentric study on home parenteral nutrition in advanced cancer patients. *Rivista italiana di Nutrizione Parenterale ed Enterale* 2002;**20**:98–107.

Keane 2018 *{published data only}*
Keane N, Fragkos K, Patel P, Bertsch F, Mehta J, Di Caro S, et al. Performance status, prognostic scoring, and parenteral nutrition requirements predict survival in patients with advanced cancer receiving home parenteral nutrition. *Nutrition and Cancer* 2018;**70**(1):73–82.

King 1993 *{published data only}*
King LA, Carson LF, Konstantinides N, House MS, Adcock LL, Prem KA, et al. Outcome assessment of home parenteral nutrition in patients with gynecologic malignancies: what have we learned in a decade of experience?. *Gynecologic Oncology* 1993;**51**:377–82.

Mercadante 1995 *{published data only}*
Mercadante S. Parenteral nutrition at home in advanced cancer patients. *Journal of Pain and Symptom Management* 1995;**10**:476–80.

Pironi 1997 *{published data only}*
Pironi L, Ruggeri E, Tanneberger S, Giordani S, Pannuti F, Miglioli M. Home artificial nutrition in advanced cancer. *Journal of the Royal Society of Medicine* 1997;**90**(11): 597–603.

Santarpia 2006 *{published data only}*
Santarpia L, Alfonsi L, Pasanisi F, De Caprio C, Scalfi L, Contaldo F. Predictive factors of survival in patients with peritoneal carcinomatosis on home parenteral nutrition. *Nutrition* 2006;**22**:355–60.

Soo 2008 *{published data only}*
Soo I, Gramlich L. Use of parenteral nutrition in patients with advanced cancer. *Applied Physiology, Nutrition, and Metabolism* 2008;**33**:102–6.

References to studies excluded from this review

Bozzetti 2014 *{published data only}*
Bozzetti F, Santarpia L, Pironi L, Thul P, Klek S, Gavazzi C, et al. The prognosis of incurable cachectic cancer patients on home parenteral nutrition: a multi-centre observational study with prospective follow-up of 414 patients. *Annals of Oncology* 2014;**25**:487–93.

Bozzetti 2015 *{published data only}*
Bozzetti F, Cotogni P, Lo Vullo S, Pironi L, Giardiello D, Mariani L. Development and validation of a nomogram to predict survival in incurable cachectic cancer patients on home parenteral nutrition. *Annals of Oncology* 2015;**26**(11): 2335–40.

Brard 2006 *{published data only}*
Brard L, Weitzen S, Strubel-Lagan SL, Swamy N, Gordinier ME, Moore RG, et al. The effect of total parenteral nutrition on the survival of terminally ill ovarian cancer patients. *Gynecologic Oncology* 2006;**103**:176–80.

Chakraborty 2011 *{published data only}*
Chakraborty A, Selby D, Gardiner K, Myers J, Moravan V, Wright F. Malignant bowel obstruction: natural history of a heterogeneous patient population followed prospectively over two years. *Journal of Pain and Symptom Management* 2011;**41**:412–20.

Chen 2013 *{published data only}*
Chen CJ, Shih SC, Wang HY, Sun FJ, Lu SC, Chu CH, et al. Clinical application of total parenteral nutrition in patients with peritoneal carcinomatosis. *European Journal of Cancer Care* 2013;**22**:468–73.

Chouhan 2016 *{published data only}*
Chouhan J, Gupta R, Ensor J, Raghav K, Fogelman D, Wolff RA, et al. Retrospective analysis of systemic chemotherapy and total parenteral nutrition for the treatment of malignant small bowel obstruction. *Cancer Medicine* 2016;**5**:239–47.

Diver 2013 *{published data only}*
Diver E, O'Connor O, Garrett L, Boruta D, Goodman A, Del Carmen M, et al. Modest benefit of total parenteral nutrition and chemotherapy after venting gastrostomy tube placement. *Gynecologic Oncology* 2013;**129**:332–5.

Fan 2007 *{published data only}*
Fan BG. Parenteral nutrition prolongs the survival of patients associated with malignant gastrointestinal obstruction. *Journal of Parenteral and Enteral Nutrition* 2007;**31**:508–10.

Gemlo 1986 *{published data only}*
Gemlo B, Rayner AA, Lewis B, Wong A, Viele CS, Ungaretti JR, et al. Home support of patients with end-stage malignant bowel obstruction using hydration and venting gastrostomy. *The American Journal of Surgery* 1986; **152**:100–4.

Girke 2016 *{published data only}*
Girke J, Seipt C, Markowski A, Luettig B, Schettler A, Momma M, et al. Quality of life and nutrition condition of patients improve under home parenteral nutrition: An exploratory study. *Nutrition in Clinical Practice* 2016;**31**: 659–65.

Guerra 2015 *{published data only}*
Guerra EA, Cortes-Salgado A, Mateo-Lobo R, Nattero L, Riveiro J, Vega-Pinero B, et al. Role of parenteral nutrition in oncologic patients with intestinal occlusion and peritoneal carcinomatosis. *Nutricion Hospitalaria* 2015;**32**: 1222–7.

Gupta 2015 *{published data only}*
Gupta R, Chouhan JS, Ensor J, Fogelman DR, Epner DE, Wolff AR, et al. Role of concurrent systemic chemotherapy and total parental nutrition (TPN) for the treatment of malignant small bowel obstruction (SBO). *Journal of Clinical Oncology* 2015;**33**:1.

Hoda 2005 *{published data only}*
Hoda D, Jatoi A, Burnes J, Loprinzi C, Kelly D. Should patients with advanced, incurable cancers ever be sent home with total parenteral nutrition? A single institution's 20-year experience. *Cancer* 2005;**103**:863–8.

Mercadante 1995a *{published data only}*
Mercadante S. Bowel obstruction in home-care cancer patients: 4 years experience. *Support Care Cancer* 1995;**3**: 190–3.

Mercadante 2015 *{published data only}*
Mercadante S, Caruselli A, Villari P, Girelli D, Prestia G, Giarratano A. Frequency and indications of parenteral nutrition in an acute palliative care unit. *Nutrition and Cancer* 2015;**67**:1010–3.

Naghibi 2015 *{published data only}*
Naghibi M, Smith TR, Elia M. A systematic review with meta-analysis of survival, quality of life and cost-effectiveness of home parenteral nutrition in patients with inoperable malignant bowel obstruction. *Clinical Nutrition* 2015;**34**:825–37.

Oh 2014 *{published data only}*
Oh SY, Jun HJ, Park SJ, Park IK, Lim GJ, Yu Y, et al. A randomized phase II study to assess the effectiveness of fluid therapy or intensive nutritional support on survival in patients with advanced cancer who cannot be nourished via enteral route. *Journal of Palliative Medicine* 2014;**17**: 1266–70.

Pasanisi 2001 *{published data only}*
Pasanisi F, Orban A, Scalfi L, Alfonsi L, Santarpia L, Zurlo E, et al. Predictors of survival in terminal-cancer patients with irreversible bowel obstruction receiving home parenteral nutrition. *Nutrition* 2001;**17**:581–4.

Szefel 2016 *{published data only}*
Szefel J, Kruszewski WJ, Szajewski M, Ciesielski M, Sobczak E, Czerepko M, et al. Medium-chain triglycerides/ long-chain triglycerides versus long-chain triglycerides in treatment of cancer patients with major body mass loss. Survival in patients with refractory cachexia. *Przeglad Gastroenterologiczny* 2016;**11**:181–6.

Tang 1995 *{published data only}*
Tang E, Davis J, Silberman H. Bowel obstruction in cancer patients. *Archives of Surgery* 1995;**130**:832–6.

Tunca 1981 *{published data only}*
Tunca JC. Impact of cisplatin multiagent chemotherapy and total parenteral hyperalimentation on bowel obstruction caused by ovarian cancer. *Gynecologic Oncology* 1981;**12**: 219–21.

Vashi 2014 *{published data only}*
Vashi PG, Dahlk S, Popiel B, Lammersfeld CA, Ireton-Jones C, Gupta D. A longitudinal study investigating quality of life and nutritional outcomes in advanced cancer patients receiving home parenteral nutrition. *BMC Cancer* 2014;**14**: 593.

Villares 2001 *{published data only}*
Villares JM, Gomis PM, Valero MA, Leon-Sanz M. Home parenteral nutrition in advanced cancer patients with intestinal obstruction or dysfunction. A single-institution experience. *Rivista Italiana di Nutrizione Parenterale ed Enterale* 2001;**19**:28–31.

Villares 2004 *{published data only}*
Villares JMM, Gomis PM, Valero MA, Leon-Sanz M. Home parenteral nutrition in patients with advanced cancer: experience of a single centre over ten years. *Nutricion Hospitalaria* 2004;**19**:253–8.

References to ongoing studies

Dreesen 2012 *{published data only}*
Prospective non-interventional non-controlled multicenter observational study to evaluate the quality of care for adult patients on HPN. Ongoing study May 2012.

Additional references

Aaronson 1993
Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez N J, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *Journal of the National Cancer Institute* 1993;**85** (5):365–76.

Anthony 2007
Anthony T, Baron T, Mercadante S, Green S, Chi D, Cunningham J, et al. Report of the clinical protocol committee: development of randomized trials for malignant bowel obstruction. *Journal of Pain and Symptom Management* 2007;**34**(1 Suppl):S49–59.

Bakker 1999
Bakker H, Bozzetti F, Staun M, Leon-Sanz M, Hebuterne X, Pertkiewicz M, et al. Home parenteral nutrition in adults: a European multicentre survey in 1997. ESPEN-Home Artificial Nutrition Working Group. *Clinical Nutrition* 1999;**18**(3):135–40.

Bielawska 2017
Bielawska B, Allard JP. Parenteral nutrition and intestinal failure. *Nutrients* 2017;**9**(5):E446.

Bozzetti 2009
Bozzetti F, Arends J, Lundholm K, Micklewright A, Zurcher G, Muscaritoli M. ESPEN Guidelines on parenteral nutrition: non-surgical oncology. *Clinical Nutrition* 2009; **28**:445–54.

Brandt 2017
Brandt CF, Hvistendahl M, Naimi RM, Tribler S, Staun M, Brøbech P, et al. Home parenteral nutrition in adult patients with chronic intestinal failure: the evolution over 4 decades in a tertiary referral center. *Journal of Parenteral and Enteral Nutrition* 2017;**41**(7):1178–87.

Brett 1986
Gemlo B, Rayner AA, Lewis B, Wong A, Viele CS, Ungaretti JR, et al. Home support of patients with end-stage malignant bowel obstruction using hydration and venting gastrostomy. *American Journal of Surgery* 1986;**152** (1):100–4.

British Intestinal Failure Alliance 2016
British Intestinal Failure Alliance. British Intestinal Failure Alliance (BIFA) position statement 2016: home parenteral

nutrition. British Association of Parenteral and Enteral Nutrition 2016; Vol. http://bit.ly/2qfFEbW (accessed 18 April 2018).

Chan 2011
Chan R, Webster J, Marquart L. Information interventions for orienting patients and their carers to cancer care facilities. *Cochrane Database of Systematic Reviews* 2011, Issue 12. DOI: 10.1002/14651858.CD008273.pub2

Cousins 2016
Cousins SE, Tempest E, Feuer DJ. Surgery for the resolution of symptoms in malignant bowel obstruction in advanced gynaecological and gastrointestinal cancer. *Cochrane Database of Systematic Reviews* 2016, Issue 1. DOI: 10.1002/14651858.CD002764.pub2

Daniele 2015
Daniele A, Ferrero A, Fuso L, Mineccia M, Porcellana V, Vassallo D, et al. Palliative care in patients with ovarian cancer and bowel obstruction. *Supportive Care in Cancer* 2015;**23**(11):3157–63.

DeBernardo 2009
DeBernardo, R. Surgical management of malignant bowel obstruction: strategies toward palliation of patients with advanced cancer. *Current Oncology Reports* 2009;**11**(4): 287–92.

Deeks 2001
Deeks JJ, Altman DG, Bradburn MJ. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. *BMJ* 2001;**323**(7306):224–8.

DerSimonian 1986
DerSimonian R, Laird N. Meta-analysis in clinical trials. *Controlled Clinical Trials* 1986;**7**(3):177–88.

DiBaise 2007
DiBaise JK, Scolapio JS. Home parenteral and enteral nutrition. *Gastroenterology Clinics of North America* 2007; **36**(1):123–44.

Dibb 2017
Dibb M, Soop M, Teubner A, Shaffer J, Abraham A, Carlson G, et al. Survival and nutritional dependence on home parenteral nutrition: three decades of experience from a single referral centre. *Clinical Nutrition* 2017;**36**(2): 570–6.

Ferguson 2015
Ferguson HJ, Ferguson CI, Speakman J, Ismail T. Management of intestinal obstruction in advanced malignancy. *Annals of Medicine and Surgery* 2015;**4**(3): 264–70.

GRADEpro 2015 [Computer program]
Evidence Prime, Inc. GRADEpro Guideline Development Tool. Hamilton (ON): McMaster University, 2015.

Guyatt 2011
Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1 introduction - GRADE evidence profiles and summary of findings tables. *Journal of Clinical Epidemiology* 2011;**64**(4):383–94. DOI: 10.1016/ j.jclinepi.2010.04.026

Hardy 1998
Hardy J, Ling J, Mansi J, Isaacs R, Bliss J, A'Hern R, et al. Pitfalls in placebo-controlled trials in palliative care: dexamethasone for the palliation of malignant bowel obstruction. *Palliative Medicine* 1998;**12**(6):437–42.

Higgins 2003
Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analysis. *BMJ* 2003;**357** (7414):557–60.

Higgins 2011
Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Howard 1995
Howard L, Ament M, Fleming CR, Shike M, Steiger E. Current use and clinical outcome of home parenteral and enteral nutrition therapies in the United States. *Gastroenterology* 1995;**109**(2):355–65.

Howard 2006
Howard L. Home parenteral nutrition: survival, cost, and quality of life. *Gastroenterology* 2006;**130**(2):S52–9.

Hozo 2005
Hozo S, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Medical Research Methodology* 2005;**5**:13.

IBM corp 2015 [Computer program]
IBM Corp. SPSS statistics for windows. version 23.0. Armonk, NY: IBM corp, 2015.

Lai 2016
Lai NM, Chaiyakunapruk N, Lai NA, O'Riordan E, Pau WSC, Saint S. Catheter impregnation, coating or bonding for reducing central venous catheter-related infections in adults. *Cochrane Database of Systematic Reviews* 2016, Issue 3. DOI: 10.1002/14651858.CD007878.pub3

Laval 2000
Laval G, Girardier J, Lassauniere JM, Leduc B, Haond C, Schaerer, R. The use of steroids in the management of inoperable intestinal obstruction in terminal cancer patients: do they remove the obstruction?. *Palliative Medicine* 2000; **14**(1):3–10.

Liberati 2009
Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLOS Medicine* 2009;**6**(7):e1000100.

Mercadante 2007
Mercadante S, Casuccio A, Mangione S. Medical treatment for inoperable malignant bowel obstruction: a qualitative systematic review. *Journal of Pain and Symptom Management* 2007;**33**(2):217–23.

Parmar 1998
Parmar MK, Torri V, Stewart L. Extracting summary statistics to perform meta-analyses of the published literature

for survival endpoints. *Statistics in Medicine* 1998;**17**(24): 2815–34.

Pittiruti 2009
Pittiruti M, Hamilton H, Biffi R, MacFie J, Pertkiewicz M, ESPEN. ESPEN guidelines on parenteral nutrition: central venous catheters (access, care, diagnosis and therapy of complications). *Clinical Nutritrion* 2009;**28**(4):365–77.

Porzio 2011
Porzio G, Aielli F, Verna L, Galletti B, Razavi GS, Ficorella C. Can malignant bowel obstruction in advanced cancer patients be treated at home?. *Supportive Care in Cancer* 2011;**19**(3):431–3.

RevMan 2014 [Computer program]
Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager 5 (RevMan 5). Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Ripamonti 2008
Ripamonti CI, Easson AM, Gerdes H. Management of malignant bowel obstruction. *European Journal of Cancer* 2008;**44**(8):1105–15.

Schünemann 2011
Schünemann H, Oxman A, Vist G, Higgins J, Deeks J, Glasziou P, Guyatt G. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Smith 2016
Smith T, Naghibi M. BANS report 2016. Artificial nutrition support in the UK 2005-2015. Adult home parenteral nutrition and home intravenous fluids.. http://www.bapen.org.uk/images/pdfs/reports/bans-report-2016.pdf (accessed 06 Feb 2018).

Società Italiana Nutrizione Umana 1996
Società Italiana Nutrizione Umana. *[Livelli di Assunzione Raccomandati di Energia e Nutrienti per la papolazione Italiana]*. EDRA Medical Publisher Revisione, 1996.

UN 1948
United Nations General Assembly. Universal Declaration of Human Rights. 1948. www.refworld.org/docid/3ae6b3712c.html (accessed 21 February 2017).

US Department of Health and Human Services, 2017
US Department of Health and Human Services. Common terminology criteria for adverse events. National Cancer Institute 2017; Vol. v5.

Wanten 2011
Wanten G, Calder PC, Forbes A. Managing adult patients who need home parenteral nutrition. *BMJ* 2011;**342**: d1447.

Wilburn 2017
Wilburn J, McKenna SP, Heaney A, Rouse M, Taylor M, Culkin A, et al. Development and validation of the Parenteral Nutrition Impact Questionnaire (PNIQ), a patient-centric outcome measure for Home Parenteral Nutrition. *Clinical Nutrition* 2017;**37**:978–83.

Winkler 2016
Winkler MF, DiMaria-Ghalili RA, Guenter P, Resnick HE, Robinson L, Lyman B, et al. Characteristics of a cohort of home parenteral nutrition patients at the time of enrollment in the Sustain Registry. *Journal of Parenteral and Enteral Nutrition* 2016;**40**(8):1140–9.

References to other published versions of this review

Sowerbutts 2017
Sowerbutts AM, Lal S, Clamp A, Todd C, Jayson G, Teubner A, et al. Home parenteral nutrition for people with inoperable malignant bowel obstruction. *Cochrane Database of Systematic Reviews* 2017, Issue 10. DOI: 10.1002/14651858.CD012812

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abu-Rustum 1997

Methods	Design: retrospective cohort study Aim: to determine the efficacy of intravenous chemotherapy alone or with PN in restoring bowel function Country: USA Funding: not reported
Participants	Number: 21 Inclusion criteria: patients with advanced epithelial ovarian cancer, small bowel obstruction and salvage chemotherapy treated at Memorial Sloan-Kettering Cancer Center 1990 to 1995 Exclusion criteria: not reported Age: mean 54.5 years (range 32 to 75) Gender: female Cancer site: advanced ovarian cancer • 16 (76%) IIIC • 3 (14%) IV • 1 (5%) IIB • 1 (5%) not defined Patients in MBO: 100% Performance status: not reported Treatment received: salvage intravenous chemotherapy • 8 paclitaxel • 7 platinum-based regimen • 6 third line single agent or combination chemotherapy (doxorubicin, ifosfamide, fluorouracil, mitoxantrone or mitomycin C
Interventions	Chemotherapy alone or in combination with PN. Details of PN solutions or nutritional aims were not reported
Outcomes	• Length of survival with or without chemotherapy: from venting gastrostomy placement
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No concealment of group allocation

Abu-Rustum 1997 (*Continued*)

Criteria for assignment to treatments	Unclear risk	Insufficient information to permit judgement
Comparability of treatment groups	Unclear risk	No details given about the two groups
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Length of survival: no missing outcome data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

August 1991

Methods	Design: retrospective case series Aim: to review the Yale-New Haven Hospital experience with HPN in MBO patients to determine the efficacy, safety, and indications for HPN in this patient population Country: USA Funding: not reported
Participants	Number 17 Inclusion criteria: patients discharged from Yale-New Haven Hospital 1980 to 1989 with MBO and receiving HPN Exclusion criteria: not reported Age: median 58 years (range 33 to 79) Gender: 13 female and 4 male Cancer site: (n) • Ovarian (9) • Colon (4) • Endometrium (1) • Appendix (2) • Stomach (1) Patients in MBO: 100% Performance status: not reported Treatment received: not reported
Interventions	HPN regimen individually designed to meet protein, calorie and fluid requirement, and avoid metabolic complications

August 1991 (*Continued*)

	HPN solution: 1.0 to 3.0 L crystalline amino acid (4.25% or 5.0%), dextrose (25% to 35%) with appropriate electrolytes, vitamins and minerals. Most patients received lipid emulsion (250 mL of 20% solution) weekly
Outcomes	• Length of survival: from date of discharge to HPN • Adverse events: readmissions from review of medical notes
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Unclear risk	Insufficient information to permit judgement
Comparability of treatment groups	Unclear risk	Only one treatment group
Blinding of participants and personnel (performance bias) All outcomes	High risk	No Blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No Blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	• Length of survival: no missing outcome data • Quality of life: no missing outcome data • Adverse events related to HPN reported in one patient and it is presumed no other adverse events occurred
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

Bozzetti 2002

Methods	Design: prospective case series Aim: to investigate changes in the quality of life in cancer patients during HPN and to determine whether it is possible to predict length of survival before administering HPN Country: Italy Funding: not reported
Participants	Number: 69 Inclusion criteria: advanced cancer patients enrolled in HPN programme from six Italian cancer centres over three years Exclusion criteria: not reported Age: mean 54 years Gender: 28 female and 41 male Cancer site: (n) • Colorectal (21) • Stomach (16) • Uterus/ovary (13) • Breast (2) • Other (17) Patients in MBO: 84% Performance status: Karnofsky performance status median 60 (40 to 90) Treatment received: 36 patients had second- or third-line chemotherapy
Interventions	HPN regimen designed to give 30 non-protein kcal/kg/day. HPN solution: Median glucose 300 g/day (160 g to 500g), median lipid 60 g/day (42 g to 100 g) and median nitrogen 12 g/day (6.2 g to 13.7g)
Outcomes	• Length of survival: measured from date of first administration of HPN • Nutritional status: measured by weight, serum albumin, lymphocyte count and serum transferrin • Quality of life: Rotterdam symptom checklist (RSCL) • Gastrointestinal symptoms: as part of RSCL
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Unclear risk	Insufficient information to permit judgement
Comparability of treatment groups	Unclear risk	Only one treatment group

Bozzetti 2002 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	• Length of survival: no missing data • Nutritional status: unclear, but presume all participants included • Quality of life: 5 participants did not complete RSCL • Gastrointestinal symptoms: 5 participants did not complete RSCL
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

Chermesh 2011

Methods	Design: prospective cohort study (two arms) Aim: to define the role of PN in patients with MBO. A group of MBO patients receiving HPN were compared to patients with HPN for other reasons; only the MBO patients are included in the review Country: Israel Funding: not reported
Participants	Number: 28 Inclusion criteria: patients 18 years or older receiving HPN discharged from Rambam Healthcare campus January 2003 to July 2009 Exclusion criteria: not reported Age: Mean 59.9 ± 12.7 years Gender: 13 female and 15 male Cancer site: (n) • Ovary (9) • Stomach (8) • Colon (4) • Pancreas (3) • Breast (2) • Squamous cell carcinoma of the larynx presumed (1) • Carcinoid presumed (1) Patients in MBO: 100% Performance status: not reported Treatment received: not reported

Chermesh 2011 (*Continued*)

Interventions	HPN given to all participants. No information was given about nutritional support aims or composition of PN solutions
Outcomes	• Length of survival: unclear how it was measured. • Adverse events: unclear how this was measured
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Unclear risk	Insufficient information to permit judgement
Comparability of treatment groups	Unclear risk	Only one treatment group was considered in the review
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	• Length of survival: no missing data • Adverse events: related to HPN reported in eight participants and it is presumed no other adverse events occurred
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

Cotogni 2017

Methods	Design: prospective cohort study (two arms) Aim: to analyse the quality of life in advanced cancer patients on HPN, and to investigate whether the combination with oncologic treatments correlates with changes in quality of life Patients on HPN receiving treatment (chemotherapy and/or radiation therapy) compared to HPN patients without treatment Country: Italy Funding: not reported
Participants	Number: 111 Inclusion criteria • Proven and prolonged failure to meet nutrition requirement by oral or enteral route • Impending risk of death due to malnutrition • Life expectancy >2 months • Karnofsky performance status (KPS) >50 • Control of pain • Absence of severe organ dysfunctions • Written informed consent confirming that the patient accepted this modality of nutrition support Exclusion criteria: not reported Age: Median 62 years (range 32 to 79) Gender: 54 female and 57 male Cancer site: (n) • Stomach (38) • Colon/rectum (21) • Pancreas/biliary system (20) • Oesophagus (10) • Lung (10) • Ovary (2) • Others (10) Patient in MBO: 80% Performance status: Karnofsky performance status, median 70 (range 60 to 80) Treatment received: chemotherapy 61, radiation therapy 2 and both treatments 9
Interventions	HPN given to all participants. No information was given about nutritional support aims or composition of PN solutions
Outcomes	• Length of survival: unclear how it was measured • Quality of life: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30. It was completed in outpatients in the presence of a healthcare professional, and then at home monthly for four months • Adverse events: unclear how this was measured
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Cotogni 2017 (*Continued*)

Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Low risk	Detailed criteria given, although there was only one treatment group
Comparability of treatment groups	Unclear risk	Only one treatment group was considered in the review
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	• Length of survival: no missing data • Quality of life: all participants accounted for but high attrition rate due to death 49/111 completed at four months • Adverse events: incidence of catheter-related bloodstream infections reported and it is presumed no other adverse events occurred
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

Duerksen 2004

Methods	Design: retrospective case series Aim: to determine whether a subgroup of participants with intestinal obstruction would benefit from support with PN Patients receiving PN at home and in hospital included in study, only HPN patients included in this review Country: Canada Funding: not reported
Participants	Number: 5 Inclusion criteria • No evidence of end-organ failure • An obstructed GI tract

Duerksen 2004 (*Continued*)

	• An estimated life expectancy longer than 2 to 3 months Exclusion criteria: not reported Age: mean 44.6 years (37 to 57) Gender: 2 female and 3 male Cancer site: (n) • Colon (3) • Gastric (2) Patient in MBO: 100% Performance status: median Karnofsky performance status 60 (50 to 70) Treatment received: chemotherapy 3
Interventions	HPN given to all participants. No information was given about nutritional support aims or composition of PN solutions
Outcomes	• Length of survival: unclear how it was measured • Adverse events: unclear how this was measured
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Unclear risk	Insufficient information to permit judgement
Comparability of treatment groups	Unclear risk	Only one treatment group
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	• Length of survival: no missing data • Adverse events: no missing data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

Finocchiaro 2002

Methods	Design: Prospective case series Aim: To assess HPN requirements, quality of life and complications in advanced cancer patients Country: Italy Funding: Not reported
Participants	Number: 70 Inclusion criteria • Being included in the ASL home-care program • Being unable to feed themselves or being unable to use enteral feeding to reach the daily nutritional requirements (absent oral feeding, or insufficient with daily nutritional requirement < 75%) • Life expectancy > 30 days • Controlled or absent pain • No severe functional damage to vital organs • Clinical and environmental conditions sustainable with home-care therapy • Informed consent from the patient and/or a relative to practice the PN • Positive feedback from the Therapeutic Unit Exclusion criteria: not reported Age: Mean 60 years (±28) Gender: 37 female, 33 male Cancer site: (n) • Stomach (16) • Pancreas/biliary system (15) • Colorectal (14) • Ovary (9) • Lungs (3) • Uterus(3) • Gut lymphoma (3) • Kidneys (2) • Other (5) Patients in MBO: 70% Performance status: Karnofsky index, median 60 (range 40 to 80) Treatment received: palliative oncologic therapy 12 (17%)
Interventions	HPN regimen designed to give energy requirements for the Italian population multiplied by specific ill factor 1.3 (Società Italiana Nutrizione Umana 1996); energy was 60% carbohydrate and 40% fat, 1.2 g/kg/day protein, 30 mL to 35 mL/kg/day fluid and micronutrients HPN solution: Initially 1500 mL/day (750 mL to 2500 mL), energy intake 1400 Kcal/day and 60 g/day protein
Outcomes	• Length of survival: unclear how it was measured • Quality of life: therapy impact questionnaire for quality of life • Nutritional status: weight, patient generated subjective global assessment • Adverse events: metabolic (hyperglycaemia and electrolyte imbalance), clinical (nausea and vomiting) and venous catheter (infections, thrombosis and catheter damage) complications were monitored. For each complication typology, duration, treatment and outcome were recorded.

Finocchiaro 2002 (*Continued*)

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Low risk	Detailed criteria given, although there was only one treatment group
Comparability of treatment groups	Unclear risk	Only one treatment group
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	• Length of survival: no missing data • Quality of life: only measured in 27 participants treated longer than two months • Nutritional status: only measured in 27 participants treated longer than two months • Adverse events: no missing data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

Keane 2018

Methods	Design: retrospective case series Aim: to examine the prognostic significance of performance status, type and site of tumour, previous or concurrent chemo-radiotherapy, anthropometric characteristics, nutritional and inflammatory status, demographic characteristics, serum biochemistry, and prognostic indices based on a large cohort of patients with advanced cancer receiving HPN at University College London Hospitals Country: England Funding: none received
Participants	Number: 107 Inclusion criteria • Adult patients, ≥18 years • Advanced cancer • Discharged on HPN from University College London Hospitals • January 1 2006 to October 15 2016 Exclusion criteria: lost to follow-up Age: Mean age 57 ± 12 years Gender: 68 females, 39 males Cancer site: (n) • Gynaecological (37) • Upper Gastrointestinal (21) • Lower Gastrointestinal (24) • Hepato-pancreatobiliary (10) • Haematological (5) • Other (10) Patients in MBO: 74.4% Performance status: Karnofsky index Mean 50 ± 16. Treatment received: 97 (90%) had chemotherapy before and/or during PN
Interventions	HPN given to all participants. Mean requirements were volume 2251 mL ± 626 mL, 11 ± 3 g/day nitrogen, 911 ± 304 kcal/day glucose, 573 ± 262 kcal/day lipid, 112 ± mmol/day sodium, 57 ± 26 mmol/day potassium, 5 ± 2 mmol/day calcium, 10 ± 5 mmol/day magnesium, 21 ±10 mmol/day phosphate
Outcomes	• Length of survival: measured from discharge until death
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Low risk	Detailed criteria given, although there was only one treatment group

Keane 2018 (*Continued*)

Comparability of treatment groups	Unclear risk	Only one treatment group
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Length of survival: no missing data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

King 1993

Methods	Design: retrospective case series Aim: to determine if HPN improved patients' nutritional parameters, survival and quality of life Country: USA Funding: not reported
Participants	Number: 61 Inclusion criteria: gynaecological cancer patients who received HPN during 1981 to 1990 and had records on the John L. McKelvey Tumor Registry or the CHAMP Home Care Program at the University of Minnesota Hospital and clinics Exclusion criteria: not reported Age: mean 55 years Gender: not reported Cancer site: • Ovarian 56% • Cervix 25% • Corpus 15% • Vulva 3% • Vagina 1% Patients in MBO: 72% Performance status: Karnofsky performance status 48 Treatment received: • Surgery 23% • Chemotherapy 51% • Radiotherapy 12%

King 1993 (*Continued*)

Interventions	HPN given to all participants. No information was given about nutritional support aims or composition of PN solutions
Outcomes	• Length of survival: date of initiation of HPN until last follow-up • Quality of life: physical and psychological well-being - level of activity, morale and presence of pain, fatigue, GI discomfort, nausea, vomiting and diarrhoea one (usual or best) to five (worse or never) scale, and Karnofsky Performance Status. Social interactions with friends and family - one (usual or best) to five (worse or never) scale. Patient employment or recreational travel - present or absent. • Nutritional status: weight, serum albumin, serum transferrin measured at one week, one month, three months, six months and one year • Adverse events: unclear how this was measured
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Unclear risk	Insufficient information to permit judgement
Comparability of treatment groups	Unclear risk	Only one treatment group
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	• Length of survival: no missing data • Quality of life: no missing data • Nutritional status: high attrition due to mortality • Adverse events: related to HPN reported in eight participants and it is presumed no other adverse events occurred
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement

King 1993 (*Continued*)

Other bias	Low risk	The study appears to be free of other sources of bias

Mercadante 1995

Methods	Design: prospective case series Aim: to describe clinical experience with HPN patients Country: Italy Funding: not reported
Participants	Number: 13 Inclusion criteria: advanced cancer patients receiving HPN at Pain Relief and Palliative Care Unit over five years Exclusion criteria: not reported Age: mean 56 years (32 to 71) Gender: 8 women and 5 men Cancer site: (n) • Pharynx (1) • Colon (4) • Stomach (1) • Breast (1) • Ileum (2) • Ovary (2) • Oesophagus (1) • Pancreas (1) Patients in MBO: 100% Performance status: not reported Treatment received: not reported
Interventions	HPN given to all participants. HPN solution: 1500 Kcal to 2000 Kcal, dextrose (approximately 60% to 70% of energy) , 10% fat emulsion (approximately 30% to 40% energy), essential amino acids enriched with branched chain L amino acids (approximately 17 g to 20 g), electrolytes and vitamins as required
Outcomes	• Length of survival: unclear how it was measured • Adverse events: unclear how this was measured • Health economic measure: cost of materials and nutrients per day
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	No randomisation

Mercadante 1995 (*Continued*)

Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Unclear risk	Insufficient information to permit judgement
Comparability of treatment groups	Unclear risk	Only one treatment group
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	• Length of survival: no missing data • Adverse events: related to HPN reported in one participant and it is presumed no other adverse events occurred • Health economic: no missing data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

Pironi 1997

Methods	Design: prospective case series Aim: to estimate the utilisation rate of home artificial nutrition (HAN); evaluate the efficacy of HAN in preventing death from cachexia, maintaining participants at home without burdens and distress to patient and family and in improving participants' performance status; and obtain information about cost-determining items of HAN Study reported on home enteral and PN patients; only HPN patients are included in this review Country: Italy Funding: not reported
Participants	Number: 29 Inclusion criteria • Hypophagia - defined as oral calorie intake absent or < 50% of basal energy expenditure • Life expectancy > 6 weeks • Suitable patient and family circumstances (pain absent or controlled, no severe vital organ failure, emotional stability, willingness and ability to cope with home artificial nutrition- related activities and suitable hygienic conditions

Pironi 1997 (*Continued*)

	• Verbal consent obtained Exclusion criteria • Absence of hypophagia • Estimated life expectancy < 6 weeks • Unsuitable home/family conditions • Lack of consent Age: not possible to distinguish between enteral and PN group Gender: not possible to distinguish between enteral and PN group Cancer site: n (%) • Head-neck 3 (10%) • Gastrointestinal 18 (63%) • Lung 1 (3%) • Genitourinary 4 (14%) • Others 3 (10%) Patients in MBO: 89% Performance status: Karnofsky performance status n (%) 30 to 40 in 9 (31%) 50 to 60 in 18 (62%) 70 to 80 in 2 (7%) Treatment received: not reported
Interventions	HPN given to all participants. No information was given about nutritional support aims or composition of PN solutions
Outcomes	• Length of survival: unclear how it was measured • Adverse events: unclear how this was measured • Health economics: cost of solutions, infusion line and dressing kits
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Low risk	Detailed criteria given, although there was only one treatment group
Comparability of treatment groups	Unclear risk	Only one treatment group
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding

Pironi 1997 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	• Length of survival: no missing data • Adverse events: related to HPN reported in three participants and it is presumed no other adverse events occurred • Health economic: no missing data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

Santarpia 2006

Methods	Design: retrospective case series Aim: to identify predictors of survival in participants with carcinomatosis on HPN Country: Italy Funding: not reported
Participants	Number: 152 Inclusion criteria: patients consecutively referred for nutrition support to Naples Clinical Nutritional Unit January 1996 to September 2003 Exclusion criteria: not stated Age: mean 57.8 years (± 13.6) Gender: 107 female and 45 male Cancer site: (n) • Stomach (48) • Ovary (42) • Colorectum (30) • Endometrium (7) • Breast (6) • Ileum (5) • Gallbladder (4) • Pancreas (3) • Kidney (2) • Skin (1) • Prostate (1) • Abdominal sarcoma (1) • Unknown (2) Patients in MBO: 100% Performance status: Karnofsky performance score in 64 participants • score $\leq$ 40 in 12 • score $\leq$ 50 in 52

	Treatment received: not stated
Interventions	HPN regimen individualised to participant's requirements containing 20 kcal/kg to 30 kcal/kg/day, 3 g to 4 g carbohydrate/kg/day, 1.0 g/kg/day lipid, 1.0 g to 1.5 g/kg/day protein HPN solution: all-in-one formula containing amino acids, glucose, lipids, minerals, trace elements and vitamins
Outcomes	• Length of survival: unclear how this was measured • Nutritional status: weight and laboratory tests
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Unclear risk	Insufficient information to permit judgement
Comparability of treatment groups	Unclear risk	Only one treatment group
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	• Length of survival: no missing data • Nutritional status: only measured in 64/152 participants surviving > 60 days
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

Soo 2008

Methods	Design: retrospective case series Aim: to describe patient-related variables in a cohort of advanced cancer patients enrolled in a HPN program Country: Canada Funding: not reported
Participants	Number: 38 Inclusion criteria • Clear cancer diagnosis • Condition that would benefit from HPN • Life expectancy in the order of months Exclusion criteria • Medically unstable • Physically or cognitively impaired • Home environment prohibiting proper treatment • Able to tolerate enteral nutrition Age: mean 48.76 years (± 13.8) Gender: 27 female and 11 male Cancer site: (n) • Ovarian (13) • Colon (6) • Gastric (6) • Peritoneal( )3 • Oesophageal (2) • Carcinoid (1) • Cervical (1) • Ampullary (1) • Gastrointestinal stromal tumours (1) • Anaplastic large lymphoma (1) • Rectal (1) • Unknown (2) Patients in MBO: 84% Performance status: Karnofsky performance score mean 62.7 (± 18.53) Treatment received: n (%) • chemotherapy 14 (36.8%) • chemotherapy + radiotherapy 2 (5.3%) • no treatment 23 (60.5%)
Interventions	HPN regimen individually designed by a registered dietitian to provide 25 kcal/kg, 1 g/kg protein and standard provision of electrolytes, trace elements, vitamins and minerals HPN solution: not reported
Outcomes	• Length of survival: unclear how it was measured • Adverse events: unclear how this was measured
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Soo 2008 (*Continued*)

Random sequence generation (selection bias)	High risk	No randomisation
Allocation concealment (selection bias)	High risk	No group allocation concealment
Criteria for assignment to treatments	Unclear risk	Insufficient information to permit judgement
Comparability of treatment groups	Unclear risk	Only one treatment group
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	• Length of survival: no missing data • Adverse events: related to HPN reported in five participants and it is presumed no other adverse events occurred
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement
Other bias	Low risk	The study appears to be free of other sources of bias

GI: gastrointestinal; HAN: home artificial nutrition; HPN: home parenteral nutrition; MBN: malignant bowel obstruction; PN: parenteral nutrition; RSCL: Rotterdam symptom checklist

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bozzetti 2014	MBO < 70%
Bozzetti 2015	Inappropriate aim for this review: Quote: "The purpose of developing and validating a nomogram to predict survival " Survival data for participants not presented
Brard 2006	Not specified that participants received PN at home

(*Continued*)

Chakraborty 2011	Only one patient had PN at home
Chen 2013	Inappropriate setting for this review: Quote: "TPN in patients with advanced-stage, incurable cancer and peritoneal carcinomatosis in a hospital setting"
Chouhan 2016	Not specified that participants received PN at home
Diver 2013	Inappropriate aim for this review: Quote: "The aim of the study is to review a single institution's experience with gastrostomy tubes"
Fan 2007	Not specified that participants received PN at home
Gemlo 1986	Received hydration and not complete nutrition
Girke 2016	Number in MBO not specified
Guerra 2015	Unable to extract data for those receiving TPN at home separately from those receiving it in hospital
Gupta 2015	Abstract for Chouhan 2016 data
Hoda 2005	Percentage of MBO <70%
Mercadante 1995a	Some participants received hydration and not complete nutrition
Mercadante 2015	MBO < 70%
Naghibi 2015	Review paper
Oh 2014	Not specified that participants received PN at home
Pasanisi 2001	Data included in Santarpia 2006
Szefel 2016	Participants received TPN in hospital
Tang 1995	MBO < 70%
Tunca 1981	Participants received TPN in hospital
Vashi 2014	Not specified that participants had MBO
Villares 2001	No outcomes relevant for review
Villares 2004	No outcomes relevant for review

MBN: malignant bowel obstruction; PN: parenteral nutrition

Characteristics of ongoing studies *[ordered by study ID]*

Dreesen 2012

Trial name or title	Prospective non-interventional non-controlled multicenter observational study to evaluate the quality of care for adult patients on HPN
Methods	Prospective observational study
Participants	Inclusion criteria: • patients in Flanders who speak Dutch; • older than 18 years; • able to give an informed consent. Exclusion criteria: • patients who are younger than 18 years.
Interventions	Aim: to give an overview of a number of aspects related to the quality of care for adult patients on HPN
Outcomes	Primary outcomes: • quality of life (time frame: 2 years) with the HPN-QoL or FACIT-G. • number of catheter-related infections (time frame: 2 years)
Starting date	May 2012
Contact information	Mira Dreesen, PhD student, PhD Student, Katholieke Universiteit Leuven, mira.dreesen@uzleuven.be
Notes	Emailed contact author and no response

HPN: home parenteral nutrition; QoL: quality of life

ADDITIONAL TABLES

Table 1. Length of Survival

Study	Numbers in study	N surviving 1 month	N surviving > 1-3 months	N surviving > 3-6 months	N surviving ≥ 6 months
August 1991	17	14	12	5	1
Chermesh 2011	68	23	14	4	3
Cotogni 2017	111	-	74[a]	38	24[b]
Duerksen 2004	5	4	4	2	2
Keane 2018	107	-	53[a]	19	19

Table 1. Length of Survival (*Continued*)

Mercadante 1995	13	3	3	2	0
Santarpia 2006	152	96	62	37	37

N=Numbers

[a] Survival was measured from 0 to 3 months in these studies.
[b] Number surviving at 9 months

Table 2. Survival for different cancer diagnoses

Study	Survival - median (range) in days				
	Ovarian cancer n = 9	Endometrial cancer n = 1	Gastrointestinal cancer n = 3	Colon cancer	Gastric cancer n = 2
August 1991	39 (10 to 77)	51	159 (106 to 208)	89 (5 to 168)[a]	
Duerksen 2004				155 (72 to 433)[b]	258 (84 to 431)

[a] n = 4
[b] n = 3

Table 3. Quality of life

Study	Numbers of participants	Timepoint	Quality of lIfe measure	Score
Bozzetti 2002	69[a]	Baseline	Rotterdam Symptom Checklist	Well-being assessment (n)[c] Very well 3 Well 55 Not well 38 Ill 0 Missing 4
	64	1 Month	Rotterdam Symptom Checklist	Well-being assessment change from baseline (n) Increased 15 No change 32 Decreased 17
Cotogni 2017	111[a]	Baseline	EORTC[b]	Mean (SD) Global QoL[d] 52 (17)
	97	1 Month	EORTC	Mean (SD) Global QoL 58 (17)
	76	2 Months	EORTC	Mean (SD) Global QoL 66 (17)

Table 3. Quality of life (*Continued*)

	54	3 Months	EORTC	Mean (SD) Global QoL 71 (14)
Finocchiaro 2002	70[a]	Baseline	Therapy impact questionnaire	Values not given
	27	2 Months	Therapy impact questionnaire	Change from baseline Deterioration 20.5% Stationary 48% Improving 31.5%

[a] Total number in the study
[b] EORTC = European Organization for Research and Treatment of Cancer Quality of life Questionnaire Core 30
[c] Number
[d] Quality of life

Table 4. Gastrointestinal symptoms

Study	Numbers in study	Numbers gastrointestinal symptoms measured	Time point	Measure	Nausea[a]	Vomiting	Gastrointestinal discomfort	Diarrhoea
King 1993	61	61	Baseline	Unvalidated [b]	3.2	-	2.8	2.0
		61	During HPN	-	2.7	-	2.4	1.8
Finocchiaro 2002	71	27	Baseline	Therapy impact questionnaire	Values not given	Values not given	-	-
		27	2 months	Therapy impact questionnaire	Change from Baseline Deterioration 26% Stationary 42% Improving 32%	Change from Baseline Deterioration 15% Stationary 57% Improving 28%	-	-

[a] Nausea and vomiting measured together
[b] 1 to 5 scale where 1 is usual or best and 5 is worse or never

Table 5. Nutritional status

Study	Numbers nutritional status measured	Timepoint	Weight (kg)	Albumin (g/dl)	Transferin (mg/dL)	Lymphocytes (x 10^9/L)	Cholesterol (mg/dL)	Haemoglobin (g/dL)	PG-SGA score (%)
Bozzetti 2002	69	Baseline	Median 52.5 (35.5 to 77.5)	Median 3.3 (2.2 to 4.8)	Median 189 (26 to 420)	Median 1.15 (0.15 to 3.05)	-	-	-
	69	Before death	Median 54.0 (36 to 78)	Median 3.2 (2.2 to 4.7	Median 180 (65 to 414)	Median 1.2 (0.24 to 3.65)	-	-	-
Finocchiaro 2002	27[a] (of 70)	Baseline	51 (37 to 76)	3.15 (1.2 to 4)	-	-	-	-	B - 33% C - 67%
	27	2 months	52.2 (40 to 71)	3.14 (1.7 to 4.5)	-	-	-	-	A - 15% B - 37% C - 48%
King 1993	61	Baseline	Mean 54.5 (13.7)	Mean 2.5 (0.6)	Mean 149 (48)	-	-	-	-
	50	1 month	Mean 57.2 (12.4)	Mean 2.4 (0.6)	Mean 149 (60.2)	-	-	-	-
	18	3 months	Mean 57.7 (11.2)	Mean 2.9 (0.6)	Mean 195 (62.2)	-	-	-	-
	9	6 months	Mean 59.8 (11.7)	Mean 3.1 (0.7)	Mean 225.4 (77)	-	-	-	-
Santarpia 2006	64[a] (of 152)	Baseline	Mean 51.7 (10.3)	Mean 3.3 (0.6)	-	Mean 1.48 (0.72)	Mean 154 (46)	Mean 11.0 (1.9)	-
	64	1 month	Mean 53.2 (10.3)	Mean 3.4 (0.5)	-	Mean 1.46 (0.67)	Mean 150 (38)	Mean 10.5 (1.9)	-

[a] Baseline values given for those patients who had nutritional status measured later.

Table 6. Adverse events

Study	Number of participants in study	Number with adverse events	Number of catheter-related bloodstream infections per 1000 catheter days
August 1991	17	1	
Chermesh 2011	28	6	
Duerksen 2004	5	1	
Finocchiaro 2002	70	7	
King 1993	61	8	
Pironi 1997	28[a]	3	
Mercadante 1995	13	1	
Soo 2008	38	5	
Cotogni 2017	111		0.33
Total	371	32	

[a] Adverse events only reported in 28 patients who died. The whole population was 29

APPENDICES

Appendix 1. MEDLINE search strategy

1. Neoplasms/
2. (neoplasm* or tumor* or tumour* or cancer* or malignan* or carcinoma* or adenocarcinoma* or carcinosarcoma* or sarcoma*).mp.
3. 1 or 2
4. exp Intestinal Obstruction/
5. ((bowel* or intestin* or gastrointestin* or gastro-intestin* or colon* or colorect* or retrosigmoid*) adj3 (obstruct* or occlu* or fail* or block* or adhes*)).mp.
6. 4 or 5
7. 3 and 6
8. exp Parenteral Nutrition/
9. (total parenteral nutrition* or TPN* or parenteral nutrition* or PN*).mp.
10. ((parenteral* or artificial* or tub* or catheter* or intraven* or IV* or subcutan* or bypas*) adj3 (nutri* or hydration* or feed* or fed* or treatment* or manag* or method* or car* or support* or diet*)).mp.
11. (home adj3 parenteral*).mp.
12. 8 or 9 or 10 or 11
13. 7 and 12

Key
mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier
pt=publication type
ab=abstract
ti=title
sh=subject heading

Appendix 2. Embase search strategy

1. Neoplasm/
2. (neoplasm* or tumor* or tumour* or cancer* or malignan* or carcinoma* or adenocarcinoma* or carcinosarcoma* or sarcoma*).mp.
3. 1 or 2
4. exp Intestine Obstruction/
5. ((bowel* or intestin* or gastrointestin* or gastro-intestin* or colon* or colorect* or retrosigmoid*) adj3 (obstruct* or occlu* or fail* or block* or adhes*)).mp.
6. 4 or 5
7. 3 and 6
8. exp Parenteral Nutrition/
9. (total parenteral nutrition* or TPN* or parenteral nutrition* or PN*).mp.
10. ((parenteral* or artificial* or tub* or catheter* or intraven* or IV* or subcutan* or bypas*) adj3 (nutri* or hydration* or feed* or fed* or treatment* or manag* or method* or car* or support* or diet*)).mp.
11. (home adj3 parenteral*).mp.
12. 8 or 9 or 10 or 11
13. 7 and 12

Key
mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier
pt=publication type
ab=abstract
ti=title
sh=subject heading

Appendix 3. CENTRAL search strategy

#1 MeSH descriptor: [Neoplasms] explode all trees
#2 (neoplasm* or tumor* or tumour* or cancer* or malignan* or carcinoma* or adenocarcinoma* or carcinosarcoma* or sarcoma*)
#3 #1 or #2
#4 MeSH descriptor: [Intestinal Obstruction] explode all trees
#5 ((bowel* or intestin* or gastrointestin* or gastro-intestin* or colon* or colorect* or retrosigmoid*) near/3 (obstruct* or occlu* or fail* or block* or adhes*))
#6 #4 or #5
#7 #3 and #6
#8 MeSH descriptor: [Parenteral Nutrition] explode all trees
#9 (total parenteral nutrition* or TPN* or parenteral nutrition* or PN*)
#10 (parenteral* or artificial* or tub* or catheter* or intraven* or IV* or subcutan* or bypas*) near/3 (nutri* or hydration* or feed* or fed* or treatment* or manag* or method* or car* or support* or diet*)
#11 home near/3 parenteral*
#12 #8 or #9 or #10 or #11
#13 #7 and #12

CONTRIBUTIONS OF AUTHORS

SB, SL, CT provided a methodological perspective.

SL, GJ, AC, AT, AMR provided a clinical perspective.

AMS, JS, AC, SL, CT screened references

AMS, JS, LH extracted data

AMS, SB, JS wrote the review.

AMS, SL, JS, AC, CT, GCJ, AT, AMR EJS, LH, SB interpretation of data and commented on the review.

SB, SL, CT, AC secured funding for the review.

DECLARATIONS OF INTEREST

Anne Marie Sowerbutts: none known

Simon Lal: none known

Andrew Clamp: none known

Chris Todd: none known

Gordon Jayson: none known

Antje Teubner: none known

Anne Marie Raftery: none known

Eileen J Sutton: none known

Jana Sremanakova: none known

Sorrel Burden:none known

Lisa Hardy: none known

SOURCES OF SUPPORT

Internal sources

- University of Manchester, UK.
- The Christie NHS Foundation Trust, UK.
- Salford Royal Foundation Trust, UK.
- University of Bristol, UK.

External sources

- Marie Curie, UK.

Marie Curie Research Grants Scheme

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We made it explicit that single-arm studies were included and participants only receiving intravenous fluids and not PN were excluded.

We planned to conduct searches incorporating both qualitative and quantitative search terms. However, we conducted a generic search for malignant bowel obstruction (MBO) and parenteral nutrition (PN) which would include qualitative and quantitative studies.